



Relationship between Depression, Quality of Life and Foot Ulcer Healing Rates in Type 2 Diabetic (T2D) Patients

A thesis submitted in fulfilment of the requirements for the degree of Master of Science

Andrew Peter Steel

B.Sc The University of Melbourne
B.P&O (Hons) LaTrobe University

College of Science, Engineering and Health

School of Health and Biomedical Sciences

RMIT University

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**Declaration**

I certify that except where due acknowledgement has been made, the work is that of the author alone; the work has not been submitted previously, in whole or in part, to qualify for any other academic award; the content of the thesis is the result of work which has been carried out since the official commencement date of the approved research program; any editorial work, paid or unpaid, carried out by a third party is acknowledged; and, ethics procedures and guidelines have been followed.

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List of Abbreviations

ADA	American Diabetic Association
CDCP.....	Centers for Disease Control and Prevention
CES-D.....	Centre for Epidemiologic Studies Depression Scale
CN.....	Charcot Neuroarthopathy
DM.....	Diabetes Mellitus
DFU.....	Diabetic Foot Ulcer
HbA1C.....	Glycated Haemoglobin (Diabetes Level)
HRFS.....	High Risk Foot Service
IDF.....	International Diabetes Federation
NHMRC.....	National Health and Medical Research Council
NICE.....	National Institute for Clinical Excellence
PAD.....	Peripheral Arterial Disease
PN.....	Peripheral Neuropathy
QoL.....	Quality of Life
TCC.....	Total Contact Cast
T2D.....	Type 2 Diabetes
WHOQOL....	World Health Organisation Quality of Life

Publications

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Abstract

Type 2 diabetes (T2D) prevalence is increasing, not only in Australia, but also worldwide. Often referred to as the ‘lifestyle disease of the 21st century’, the impact it has on individuals can be profound. A significant co-morbidity and the most common complication of T2D is foot ulcers. There is an established relationship between depression and T2D; however, no studies have investigated this relationship amongst a population with a diabetic foot ulcer (DFU). This study’s aim was to investigate the relationship between different levels of depressive symptoms, Quality of Life (QoL), and healing time of people with T2D and a DFU. The relationship between different levels of T2D on healing time of foot ulcers and QoL was also explored. The study’s sample was drawn from a High Risk Foot Service (HRFS) at Northern Health, Victoria, Australia. All participants had T2D and a neuropathic foot ulcer. The sample participants; 59 males and 22 females, with a mean age of 62.6 years (SD = 12.2, range of 21 years to 85 years), were assessed for their level of depressive symptoms using the Center for Epidemiologic Studies Depression scale and their QoL using the World Health Organisation Quality of Life BREF scale. Significant relationships were found between different levels of depressive symptoms, healing time and QoL. Higher levels of depressive symptoms correlated with longer healing time. T2D levels had no significant relationship with healing time or QoL; however, T2D levels mediated the direct relationship between depressive symptoms and healing time. Healing time was found to be inversely related to all measures of QoL. The clinical significance of these results is relevant, in providing insight into the relationship that depressive symptoms and QoL have with the healing time of diabetic foot ulcers. These results also suggest that treatment approaches incorporating the treatment of depression and improving QoL.

Chapter I: Introduction

This chapter will commence with a thesis overview, then introduce the research undertaken, providing some initial background to the topic, and concluding with an outline of the rationale for this project and the research aims.

1.1 Thesis Overview

Chapter one will contain the background and rationale of the study with the research objectives and research questions that will be derived from the rationale of the study. The scope and significance of the study, along with a brief thesis overview will be outlined. Chapter two will review the recent relevant literature to provide a more detailed background on the evidence of the relationship between depression and T2D. Research outlining the mechanism of the biological relationship linking depression and T2D will be explored, along with evidence on screening for depression, diabetic foot ulcers; causes and costs, measuring depression and moving forward to the issues of depression amongst people with T2D, and how this impacts those with a DFU. This chapter will analyse the impact of T2D on society more broadly, and the relationship that is already established between T2D and depression.

Chapter three will present the methodological approach undertaken in this research. This chapter will go into details on how the research questions will be answered. It will outline in detail the eligibility of participants and how they were recruited. Details of the questionnaires will be provided and reasons why the Centre for Epidemiologic Studies Depression Scale (CES-D) and the World Health Organisation Quality of Life (WHOQOL) BREF scale were used in this research. Details will also be provided on the data collection for the variables of treatment time, and blood glucose levels to indicate the level of T2D. This chapter will outline how the data was to be analysed, and the specific relationships and outcomes that were to be investigated.

Chapter four will present the data analysis. This chapter will start broadly with the descriptive analysis of the data collected, and the associated findings. Data will be presented to address each of the outlined aims. Chapter five will discuss an interpretation of the findings obtained, why these findings are relevant to the research and how they relate to other existing research. Chapter six will state the conclusions of the study's aims and provide a summary of the complete research study, along with a series of recommendations.

1.2 Background of Study

Diabetes mellitus (DM), also referred to as diabetes or type 2 diabetes (T2D), is the most common non-communicable disease that affects millions of people worldwide. Type 2 diabetes has also been deemed the most emergent epidemic in more newly industrialized and developing nations. Its prevalence is increasing, not only in Australia, but also worldwide. Often referred to as the 'lifestyle disease of the 21st century', the impact it has on the cost of public health and society has increased rapidly (Houghton, 2015). Regardless of the increasing awareness of T2D, it continues to represent both a national and global health challenge. Over 500 data sources between 1980 and 2011 were reviewed, with 170 sources of T2D prevalence analysed from 110 countries; with the rate of T2D in 2011 estimated at 366.2 million with a forecasted rate of 551.8 million by 2030 (Whiting, Guariguata, Weil & Shaw, 2011). With the prevalence increasing daily, more than 80% of people now diagnosed are from low and middle-income countries. From 1980 to 2011, 4.6 million deaths were attributed to T2D by 2011 (Whiting et al., 2011). Other population based studies have also projected an increase rate of T2D in young adults, which will subsequently lead to the increase in micro and macro vascular complications of T2D (Alberti et al., 2004). Type 2 diabetes is a serious health condition that requires the attention of public health interventions as well as improvement of intervention at the clinical level (Sandeep, Ganesan, & Mohan, 2010; Whiting et al., 2011).

Type I diabetes is characterised by the body's inability to produce insulin and hence requires a constant supply of insulin. Type 2 diabetes on the other hand is primarily the body's cells inability to use the normal insulin that is produced, due to a developed resistance which leads to the body producing excessive insulin or can be due to an insufficiency of insulin production (Pillai, 2012). Due to this the blood glucose levels rise and with uncontrolled hyperglycemia over a long period, this leads to the damage of several organs such as the kidney, blood vessels, heart, eyes and nerves (Diabetes Australia, 2016). Hyperglycaemia also makes people with T2D prone to infection (Diabetes Australia, 2016).

Several high-income countries are now faced with increased incidence of cardiovascular diseases, kidney failure, lower limb amputation and even blindness as a direct result of T2D (WHO., 2017). Nerve and blood vessel damage is also observed, leading to problems in the foot. The foot condition tends to become worse in the presence of infection and thus leads to the formation of an ulcer. Subsequently the individual with T2D then becomes more susceptible to lower limb amputation. People with T2D are 25 times more likely to undergo lower limb amputation than those without T2D (Davis, Stratton, Fox, Holman, & Turner, 1997).

Foot ulcers are a significant co-morbidity of T2D. They are the most common complication, affecting 60-70% of patients admitted to hospital with T2D (Charnogursky, Lee, & Lopez, 2014) Peripheral neuropathy of the feet increases the risk that abrasions go undetected and leads to an ulcer. Type 2 diabetes affects people's feet in a number of ways; peripheral numbness or neuropathy is common (Charnogursky, Lee, & Lopez, 2014). They are more susceptible to pressure with less flexibility of the joints in their feet, they have dryer and more fragile skin, and decreased blood flow resulting in delayed healing of cuts and abrasions.

Diabetic foot ulcers (DFU), have been found to be the largest cause of increasing costs and hospital admission for people with T2D. It is established that 12-25% of all people

with T2D will at some stage develop a DFU (Chung, 2007). The impact of having a DFU on many aspects of life is significant, and this impact is an area that warrants thorough and further investigation.

1.3 Rationale of the Study

A DFU has been established as a common complication of having T2D, and there is no evidence that the length of time an individual has had T2D influences DFU healing time (AlGoblan, Alrasheedi, Basheir & Haider, 2016). Patients with DFUs are severely limited in their physical function, have an impaired health status and a poorer health related quality of life (QoL) compared to people without T2D and a DFU (Evans & Pinzur, 2005). Depression is frequently linked to diabetic complications (Wexler et al., 2006). Although neither the mechanism for the co-occurrence of T2D and depression nor the directional pattern of causality are yet known, their relationship and implications are clear (Hu, Amoako, Gruber & Rossen, 2007). The potential to accelerate T2D complications is significant; further enhanced by recent advancements in research showing a biological link between depression and T2D symptoms (Golden et al., 2008). This makes the clinical management of DFUs more complex. Studies have found that depression is quite common in patients with a DFU and associated with an increase in treatment cost with an added risk of hospital admission and mortality (Ismail, Winkley, Stahl, Chalder, & Edmonds, 2007; Vileikyte, Rubin & Leventhal, 2004). Health related QoL is also seen to be lowered coupled with a decline in health status (Goodridge, Trepman, & Embil, 2005).

Health related QoL is impacted through a decrease in mobility and the ability to carry out daily activities (Evans & Pinzur, 2005). Previous research by Rubin and Peyrot (1999) has confirmed that patients with DFUs are adversely affected both psychologically, as well as socially due to a reduction in carrying out social activities and increased family tension both for the caregivers as well as the patients themselves. There is also the added difficulty of

employment and financial hardship, reported by qualitative studies. Quantitative studies on the other hand reiterate the findings of the explorative studies that DFU have a negative impact on the social and psychological functioning of the patient (Goodridge et al., 2005; Rubin & Peyrot, 1999).

Thirty one percent of adults with T2D have comorbid depression (Ciechanowski, Katon, Russo, & Hirsch, 2003). This association of T2D with depression is associated with a worsening of several clinical factors of T2D such as poorer glycemic control and the magnification of other symptoms (Ciechanowski et al., 2003). Additionally, the prevalence of the complications increases (Lin et al., 2010). Furthermore, in these patients a worsening of physical and cognitive functions, a reduced adherence to dietary recommendation (Ciechanowski et al., 2003) and medication with a lowered QoL is also observed (Grandy, Chapman, & Fox, 2008). Due to the significant impact of depression on the clinical outcomes in patients with T2D, an evaluation of the psychological status, as well as the depressive symptoms has been highly recommended (International Diabetes Federation, 2005). These recommendations however have not been carried out effectively in clinical practice. The treatment of these comorbidities is essential for effective clinical management (Ciechanowski et al., 2003).

While studies have shown significant association of DFU with depression (De Groot, Anderson, Freedland, Clouse, & Lustman, 2001), the studies have not shown an association between the DFU and its outcomes. Even though depression has been continuously and adversely associated with DFU, its effects on self-care, foot care and its role in the prevention of DFU further has only been minimally explored (Gonzalez, Peyrot, et al., 2008; Gonzalez, Safren, et al., 2008; International Working Group on the Diabetic Foot, 1999; National Institute for Clinical Excellence, 2004).

The rationale for this research is that currently there is a well-established relationship between depression and T2D. A large amount of research has investigated this relationship,

and the influence depression and T2D have on QoL. However, to date there has been little research investigating the relationship between levels of depression and DFUs, and no research specifically exploring at the relationship between depressive symptoms and DFU healing rates. It is acknowledged from the literature that depressive symptoms negatively impact on individuals QoL, however the relationship between depressive symptoms and QoL amongst a population with a DFU is not well understood. Any relationship or influence depressive symptoms have on T2D levels amongst a population with a DFU will also be investigated as current literature does not specifically consider this relationship within this defined population.

1.4 Aims of Research

The primary purpose and aim of conducting this research was:

1. To determine if there is a relationship between depressive symptoms and the healing time of DFUs.

The secondary aims of this research was:

2. To determine if there is a relationship between depressive symptoms, severity of T2D and the healing time of a DFU.
3. To determine if there is a relationship between depressive symptoms on the QoL amongst people with a DFU.

1.5 Scope and Significance of the Study

While well established the interaction between depression and DFUs, the relationship that both of these have with QoL has not been explored (Vileikyte et al., 2005; Vileikyte et al., 2009). It has been noted that with a decrease in QoL, the psychological impact of T2D increases and this also manifests with a negative influence on the self-care of the patient (Gask, Ludman, & Schaefer, 2006). While depression levels have adverse impact on activity levels, more research exploring such an association is warranted. Here the integration of

mental health specialists as part of the treatment of patients with a DFU may enhance the outcome of the QoL for those with a DFU. Early recognition and intervention for depression in people with T2D may improve the healing rates when a DFU occurs, and also reduce the cost of healthcare (Vileikyte et al., 2005) both for the patients as well as for the health care providers.

Chapter II: Literature Review

2.1 Introduction

The fact that adults aged 20-70 years are increasingly afflicted with T2D is a global health concern (Bloom et al., 2011). From 135 million in 1995 the number of people with T2D is predicted to rise up to 300 million by 2025 (King, Aubert, & Herman, 1998). In developed countries the rate of increase is 42%, but developing countries are expected to witness a 170% increase in prevalence of T2D. In developing countries worldwide 75% of people may have T2D by the year 2025 (King et al., 1998). The prevalence of T2D is found to be increasing amongst the Asian population because of economic development, nutrition transition and sedentary lifestyles. In 2007, Asia was home for around 110 million individuals with T2D, with young and middle aged people disproportionately affected (Chan et al., 2009). These proposed increases in T2D create a massive global health challenge.

2.2 T2D, Foot Ulcers and their Management

People with T2D are normally prone to foot infections, which have their own serious sequelae. The factors which contribute to the growth of this problem are the ongoing rise in incidence of T2D in developed and lesser-developed countries, the increasing body weight of patients with T2D and their greater longevity through modern medicine and treatments (Hu et al., 2007). Skin ulceration as a consequence of peripheral (sensory and motor) neuropathy, which allows the unconscious formation of a wound caused by some form of trauma is the root cause of a DFU (Armstrong, et al., 2001; Boyko, et al., 1999). Microorganisms often colonize these wounds leading to tissue damage and infection. These infections then spread into deeper tissues and finally reach bone in most cases. Even a mild DFU can cause major morbidity, physical and emotional distress, loss of mobility and significant direct and indirect financial costs (Hu et al., 2007). In the case of prolonged and worse infections hospitalisation, surgical resection or even amputation may become essential, as an only

effective treatment option (Armstrong, Wrobel, & Robbins, 2007). Foot ulcers have been found to have a prevalence of 1-4% in patients with T2D and have been found to be the highest cause for leg amputation in cases of non-trauma (Doupis et al., 2008).

The main reason for T2D related hospitalisation and lower extremity amputation is diabetic foot complications and their associated infections. According to the latest data from the US Centers for Disease Control and Prevention (CDCP), the number of hospitalisation for diabetic foot “ulcer/infection/inflammation” rose from 1980 to 2003. The total number crossed 111,000 and surpassed the number attributed to Peripheral Arterial Disease (PAD) (CDCP, 2010c) In the early 1990s the annual number of hospital discharges for nontraumatic lower extremity amputations as a result of DFUs and infections rose steadily. By 2005, hospital admissions had leveled off to 71,000 (CDCP, 2010b) with improvements in early treatment and infection control alone, thus demonstrating that early identification and management of a DFU is critically important to the overall success of DFU treatment.

Over the past decade the annual rate of amputations in the United States reduced to half of its previous rate. The new rate was 4.6 per 1000 persons who have T2D. This was due to improvements in infection control and T2D management (CDCP, 2010a). The decrease was most significant for major above the ankle amputations (CDCP, 2010a). The inferences observed in the United States, however, differ from a recent study in the United Kingdom, which found that the number of amputations in patients with Type 1 diabetes decreased between 1996 and 2005, yet the number of such occurrences for patients with T2D has nearly doubled. Major amputations increased more than 40%. While several factors were identified for the decrease, T2D prevention strategies and controlling for infection were the most prominent factors (Vamos, Bottle, Majeed, & Millett, 2010). It was also established that people with T2D related amputations and infections, had a 5-year mortality rate consistent with that of the most fatal cancers (Armstrong, Wrobel, & Robbins, 2007).

The documenting of a clear and consistent approach to the treatment and management of DFUs in 2004 was a significant influencing factor in the improvement of amputation rates and mortality. Prior to the initial 2004 DFU treatment guidelines more than 75% of patients with a DFU had no adequate wound off-loading, or infection control, with 58% of the foot ulcers being clinically infected (Prompers et al., 2007). A follow-up study conducted one year later found that despite improvements in infection and treatment, 23% of the patients still had not healed their foot ulcer (Prompers et al., 2007). The key focus of the initial DFU guidelines, was a consistent and methodical approach to the management of DFU infections and general treatment principals, in an easily understood language which could be applied across the world. The effectiveness of following guidelines and consistent infection control practices are clear when implemented in countries such as the United States compared to the United Kingdom, as Vamos, Bottle, Majeed, and Millett, (2010) identified, where inconsistent treatment of DFU infections lead to higher amputation rates between 1996 and 2005.

Periphereal arterial disease is the first independent baseline predictor of non-healing foot ulcers (Prompers et al., 2008). For patients with PAD, infection was the main obstacle for getting their foot ulcer healed (Prompers et al., 2008). Among the four independent predictors of minor amputation in people with T2D, infection was the most significant predictor (Van Battum et al., 2011). As the severity of DFU increased, hospitalisation, antibiotic therapy and surgery were the highest costs to the patients (Prompers et al., 2008). Many DFU patients' treatment does not align with the current best practice guidelines. Different countries and centers have varied managements, the guidelines that are presently available are too general and they lack specific guidance. Guideline recommendations such as "the routine surveillance for foot problems in people with T2D should be performed once a year, and at risk feet withouth a current active problem every 3-6 months" (National Health and Medical Research Council (NHMRC), 2005, p.53) and "People with diabetes should

receive specific footcare education” (NHMRC, 2005, p.65) do not explore and detail what routine surveillance is, and what clinical measures should be reviewed. Further when referring to the ideal content, nature and frequency of education necessary to improve DFU outcomes the guidelines state these are unknown (NHMRC, 2005). This has led to inconsistent DFU outcomes in different countries as highlighted previously between the US and UK (CDCP, 2010a; Vamos et al., 2010). Recommended therapies often end up underused because of the barriers in healthcare organisations and different personal beliefs, leading to differences in successful DFU treatment outcomes (Prompers et al., 2008).

Previous studies have shown improvements in outcomes for patients with DFU over the past 20 years, with major amputation rates reduced when specialty diabetic foot clinics paid medical attention to patients. Specialised inpatient foot teams were also improving patient outcomes. The change to a multidisciplinary nature of care has been the key factor in this success. Denmark set up a multidisciplinary wound healing centre where diabetic foot care was treated as an expert discipline. The centre enshrined wound knowledge and understanding of wound problems, leading to increased success in improving healing rates of patients with leg and foot ulcers, and a decrease in the number of major amputations (Gottrup, Holstein, Jørgensen, Lohmann, & Karlsmar, 2001). If minor adjustments are made for local conditions this model can be applied to most industrialised and developing countries. A 37% reduction in the incidence of non-traumatic lower limb amputations was reported in a study from one city in Germany when data from 1990-1991 was compared to data from 1994-2005, following the use of specialised physicians along with a defined clinical pathway for DFU treatment (Trautner, Haastert, Mauckner, Gätcke, & Giani, 2007). One hospital in UK successfully reduced the amputation incidence rate by 40% and major amputations were reduced by 62% over a 11 year span following improvements including multidisciplinary team work amongst foot care services (Krishnan, Nash, Baker, Fowler, & Rayman, 2008). Adoption of simple protocols with no increased staff can result in improved

outcomes and lower costs as suggested by some of the recent studies (Hellingman & Smeets, 2008). Hospitals in small rural and underdeveloped areas also showed significant improvements in outcomes of DFUs, following the adoption and application of multidisciplinary protocols (Rerkasem et al., 2008). A study used a risk-based Markov analysis of data from Dutch studies concluded that “management of the diabetic foot according to guideline-based care improves survival, reduces diabetic foot complications, and is cost-effective and even cost saving compared with standard care” (Ortegon, Redekop, & Niessen, 2004 p.905). Guidance for inpatient management of diabetic foot problems was published by the UK National Institute for Clinical Excellence (NICE) on the basis of a systematic review of published data (Tan et al., 2011).

A care pathway should be established in every hospital for inpatients with a diabetic foot problem, break in the skin, inflammation, swelling, gangrene, or signs of infection. Professionals with the required specialist skills should form a multidisciplinary foot care team that should assess the patient’s response to medical, surgical and T2D management within 24 hours of the initial examination. Such assessment will determine the need for specialist wound care, debridement, and pressure off-loading or vascular or surgical interventions. It would also help in reviewing the treatment of any infection such as a treatment with antibiotic therapy. Other foot deformities or recurrent foot problems could be prevented if the need for specialist treatment is realised in time (Tan et al., 2011).

Although significant thought and clinical focus is placed on the prevention of diabetic foot wounds (Singh, Armstrong, & Lipsky, 2005), few studies have investigated the value of educating patients with T2D on preventative methods. One prospective controlled study provided patients with computerised information on preventive techniques (Haller, Gil, Gardner, & Whittier, 2009). Diabetic foot ulcer management strategies should involve intensive prevention, early assessment, and aggressive treatment by a multidisciplinary team

of experts to be successful; since it is a limb threatening and debilitating condition when a patient with T2D has a foot infection.

2.3 Aetiopathogenesis

A classical triad of neuropathy, ischaemia and infection lead to occurrences of DFUs (Pendsey, 2010). Since T2D marks an impaired metabolic mechanism, the risks of infection and slow wound healing is high. People with T2D will also face decreased cell and growth factor response, diminished peripheral blood flow in addition to decreased local angiogenesis (Brem & Tomic-Canic, 2007). Hence, the feet are more prone to peripheral vascular disease (PVD), damage of peripheral nerves, deformities, ulcerations, and gangrene. A decrease in nitric oxide will also lead to the constriction of the blood vessels, a propensity for atherosclerosis and eventually ischaemia (Dokken, 2008; Lüscher, Creager, Beckman, & Cosentino, 2003).

2.4 Neuropathy

More than 60% of the foot ulcers are caused by neuropathy, with both Type 1 Diabetes and T2D patients affected (Clayton & Elasy, 2009). An increase in blood glucose level results in increased enzyme production namely aldose reductase and sorbitol dehydrogenase. These enzymes are responsible for converting glucose into sorbitol and fructose. The synthesis of nerve cell myoinositol decreases when the sugar products accumulate in the body which, in turn, affects nerve conduction (Clayton & Elasy, 2009). Microangiopathy induced by hyperglycaemia causes reversible metabolic, immunologic and ischaemic injury of autonomic, motor and sensory nerves (Younger, Rosoklija, & Hays, 1998). As a result peripheral sensation decreases and the nerve innervations of small muscles of the foot and fine vasomotor control of the pedal circulation get damaged (Jeffcoate & Harding, 2003). The patient is prone to getting a minor injury when nerves are injured; the injury will most probably go unnoticed initially until it becomes an ulcer. Patients with sensory loss have a seven-fold increased risk of getting foot ulcers when compared to non-

neuropathic patients with T2D (Wild, Roglic, Green, Sicree, & King, 2004). Affected nervous system, dryness and fissuring of skin which is prone to infection are some of the aftermaths of T2D. Microcirculation of the skin is also controlled by the autonomic system. Eventually these changes lead to ulcers, gangrene and limb loss (Boyko et al., 1999; Vinik, Maser, Mitchell, & Freeman, 2003). Vasculopathy hyperglycemia causes abnormalities like endothelial cell dysfunction and smooth cell abnormalities in peripheral arteries. Changes in endothelial cells, influence the body's peripheral circulation and increased endothelium-derived callus formation (Bowering, 2001; Murray, Young, Hollis, & Boulton, 1996). Ongoing pressure coupled with more delicate skin and increased callus formation leads to skin breakdown and ulceration (Rosen, Davids, Bohanske, & Lemont, 1985). To quote Duckworth, Boulton, Betts, Franks, and Ward (1985) "abnormally high pressures are more common in patients with diabetic neuropathy and almost all patients with a history of ulceration show high-pressure areas which correlate well with the site of previous ulceration" (p. 80). Normally ulcers are seen on the plantar aspects of great toe and heel. Badly fitting shoes may also cause ulcers on the dorsal aspect occasionally which is the predominant source of trauma (Macfarlane & Jeffcoate, 1997; Peters, Armstrong, & Lavery, 2007). Neuropathic foot ulcer in T2D patients has an associated complex multifactorial aetiopathogenesis. Peripheral neuropathy compliments areas of high pressure and associated skin changes ultimately lead to ulcer formation.

2.5 Neuroarthropathy

Disturbances in sensory innervations of the affected joint cause foot deformities such as Charcot Neuroarthropathy (CN) which is a chronic painless progressive degenerative arthropathy (Rogers et al., 2011). Type 2 diabetes causes impairment of the autonomic nervous system which, in turn, leads to an increased local blood supply. The resting blood flow in T2D patients is much higher than in the normal patient. Calcium starts dissolving because of the sudden increase in blood flow; bone gets damaged and leads to osteoclastic

activity of the bone (Rogers et al., 2011). There is another theory suggested by Van Der Ven, Chapman and Bowker (2009) that states that repetitive minor trauma to the insensate joints leads to fracture and disintegration. An uncontrolled osteolysis may happen due to the production of proinflammatory cytokines (Van Der Ven et al., 2009). Tumor necrosis factor- α and interleukin-1 β are the cytokines which cause the expression of receptor activator of nuclear factor - κ b to rise (Van Der Ven et al., 2009). Subsequently the production of nuclear factor- κ b gets triggered and maturation of osteoclasts takes place leading to joint deformity (Van Der Ven et al., 2009). Midfoot collapse or “rocker-bottom” foot is the hallmark deformity identified with CN (Van Der Ven et al., 2009). Deformities such as these and any foot deformity along with neuropathy predispose T2D patients to recurrent ulcerations at higher rates (Van Der Ven et al., 2009). Deformities cause either plantar pressure points or footwear pressure points, and the lack of sensation to constant pressure leads to skin breakdown and ulceration (van Schie, Vermigli, Carrington, & Boulton, 2004).

2.6 Depression and Diabetes

The term depression is used in many different ways; from describing transient states of low mood experienced by most if not all people at some time in their life, through to a severe psychiatric disorder (National Health Priority Areas Report, 1999). The terms depression and depressive symptoms in this thesis will refer to a participant’s depressed or sad mood, associated with the following symptoms: a loss of interest or pleasure in one’s usual activities, thoughts of worthlessness or changes in appetite and/or sleep patterns, along with the associated symptoms as defined by the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) 5th Edition.. Depression is now established as the leading cause of disability around the world (Eagle, 2017). Over the past 20 years, a number of studies including meta-analyses and systematic reviews have consistently shown that the prevalence of depression in people with T2D is 2-3 times greater than those without T2D (Ali, Stone, Peters, Davies, & Khunti, 2006; Anderson, Freedland, Clouse, & Lustman, 2001; Lloyd et al.,

2010; Pouwer et al., 2010). Vileikyte et al. (2005) specifically examined the relationship between diabetic neuropathy and depression. The study employed the use of clinical rating scales in 494 patients with diabetic neuropathy. They found a significant relationship between depression and diabetic peripheral neuropathy.

A review by Andreoulakis, Hyphantis, Kandylis and Iacovides (2012) discussed the incidence of comorbid disorders in patients with T2D. It was determined that the prevalence of a mental health disorder in people with T2D is higher when compared to those without T2D, particularly depression. The review also stated that the exact pathophysiology of depression in people with T2D is unknown (Andreoulakis et al., 2012). However, depression remains an immensely important comorbidity that must be considered in this population, as it is known to decrease health related QoL. The negative impact of depression on an individual's QoL leading to functional decline, plus the additional burden it has on family members and caregivers is well established. Through influencing sleep, to loss of appetite, constant fatigue and body aches, depression was found to negatively impact on many facets of both individual's and family members QoL (Arroyo et al., 2004; Carnethon et al., 2007; Carnethon, Kinder, Fair, Stafford, & Fortmann, 2003; De Groot et al., 2001; Eaton, Armenian, Gallo, Pratt, & Ford, 1996; Engum, 2007; Everson-Rose et al., 2004; Golden et al., 2004; Kawakami, Takatsuka, Shimizu, & Ishibashi, 1999; Lustman et al., 2000; Palinkas, Lee, & Barrett-Connor, 2004). A number of studies have highlighted that depressive symptoms reduced the QoL in people with T2D due to somatic symptoms and complications (Hu et al., 2007; Katon, Lin, & Kroenke, 2007; Paschalides et al., 2004). These symptoms have been linked with both metabolic and behavioral risk factors for T2D (Peyrot & Rubin, 1997). Furthermore, people with depression are less likely to comply with dietary advice (Marcus, Wing, Guare, Blair, & Jawad, 1992) are more likely to be physically inactive, (Arroyo et al., 2004; Carnethon et al., 2007, 2003; Engum, 2007; Everson-Rose et al., 2004) and thus have an increased risk of obesity, which further exacerbates their T2D. This

corroborates findings from earlier studies that depressed individuals have higher caloric intake (Golden et al., 2004, 2007) and are less physically active (Arroyo et al., 2004; Carnethon et al., 2007, 2003; Engum, 2007; Everson-Rose et al., 2004).

One of the most significant longitudinal studies conducted over 21 years, established that participants who were found to have the highest levels of depressive symptoms, developed the highest levels of reported T2D over time, from baseline (Carnethon et al., 2003). The very large sample size and length of study undertaken by Carnethon et al. (2003) carries significant weight, with its conclusions, validity and reliability into the mediating effect of depression upon T2D. Participants who developed higher levels of depressive symptoms over the 21 years were found to be at an elevated rate of 2.52 times more likely to develop T2D (Carnethon et al., 2003). The main limitation of this study was that T2D levels were only assessed by self-report or from medical records and not an objective biochemical test such as the glycated haemoglobin (HbA1C) test.

Georgios et al., (2013) outlined the issues related to comorbidities in people with T2D, and how important it is to prevent these to improve treatment outcomes amongst this population. The authors stated that prevention of such conditions as mental fatigue, coronary artery disease, and depression are important to maintain good glycaemic control, and to improve the T2D and its associated comorbidities. Another review by Markowitz, Gonzalez, Wilkinson, and Safren (2011) offered evidence that depression is very much prevalent in people with T2D, and that this is the most significant comorbidity that needs addressing in people with T2D. The review was systematic in nature and included 17 studies that specifically treated depression in patients with T2D, with modalities including cognitive behaviour therapy, psychosocial interventions, and anti-depressants.

Amongst the elderly population T2D rarely exists in isolation (DiMatteo, Lepper, & Croghan, 2000) with impairment, disability and higher rates of complications found in patients with both depression and T2D compared to people with either one of these

conditions (Caruso, Silliman, Demissie, Greenfield, & Wagner, 2000; DiMatteo et al., 2000; Ismail, 2009; Katon & Ciechanowski, 2002). This is further supported by past research indicating a positive relationship between depression and T2D, with depressive symptoms associated with an exacerbation and acceleration of the onset of T2D symptoms and complications (Black, 1999; Ismail, 2009; Leedom, Feldman, Procci, & Zeidler, 1991; Lloyd, Matthews, Wing, & Orchard, 1992; Musselman, Betan, Larsen, & Phillips, 2003; Padgett, 1993). Interesting findings by Golden et al. (2008) found that the association between T2D and depression was not the same for all individuals, and that it varied with the treatment of T2D. The suggestion was that requirements in monitoring and treating an individual's T2D may lead these individuals to have elevated depressive symptoms compared to those who did not treat their T2D (Golden et al., 2008). Further research has found the association between T2D and incidents of depressive symptoms decreased following an adjustments for T2D comorbidities (Maraldi et al., 2007), thus suggesting that complications of T2D may be more influential in developing depressive symptoms than T2D itself.

2.7 Biological Relationship

Golden et al. (2008) stated that the biological mechanisms by which depression and T2D are associated remains unclear despite research indicating a bidirectional association between these two chronic conditions. Numerous studies allude to linking these two conditions by an inflammatory response at a cellular level (Bastard et al., 2006; Kiecolt-Glaser & Glaser, 2002), which increases the activation of the hypothalamic-pituitary-adrenal axis. Some population studies conducted by Ford (2002) and Schmidt et al (1999) have reported that this inflammation is associated with the development of T2D through limiting insulin uptake, leading to insulin resistance (Bastard et al., 2006; Black, 2003; Ford & Erlinger, 2004; Kiecolt-Glaser & Glaser, 2002; Musselman et al., 2003). One suggested association is that obesity or atherosclerosis is associated with low-grade inflammation prior to the onset of T2D (Carnethon et al., 2003; Pouwer et al., 2010).

2.8 Depression and Diabetes Self-Care

Effects of depressive symptoms on a client's ability to self-care have been explored (Vickers, Nies, Patten, Dierkhising, & Smith, 2006) with symptoms such as reduced energy, appetite, and motivation, plus the cognitive effects associated with depression, impacting on the individual's ability to self-care (Lloyd et al., 2010). The term 'diabetes burnout' was coined by Barnard, Peyrot and Holt (2012) to report the feeling of T2D controlling people's lives, including being overwhelmed and defeated by T2D and frustrated by the required self-care regime (Barnard et al., 2012; Vickers et al., 2006).

There is some limited evidence that interventions to improve depression lead to improvements in general health outcomes (Jackson, DeZee, & Berbano, 2004); however, other studies have shown that significant improvements in depression levels do not always lead to improved glycemic control (Gask, Ludman, & Schaefer, 2006). The almost exclusive focus in previous research on the burden of managing T2D, and the impact on an individual's ability to self-care, has according to Vileikyte et al. (2004) neglected to include the chronic complications of T2D and their effects on an individual's mental health. There is evidence that by improving other co-morbidities of T2D, it is possible to improve depression levels and the ability to self-care, while also reducing the impact of T2D (Carnethon et al., 2007; Golden et al., 2008). Complications of T2D, such as neuropathy and subsequent DFUs, have a significant impact on patients' adherence behaviors, not just their ability to self-care (Vileikyte et al., 2004). Research into these adherence behaviors has led to improvements in the methods of education and the information that is delivered to patients, with an aim to empower individuals in the management of their condition. When patients can be effectively engaged in their treatment, and responsibility for their own care is promoted, health outcomes have been shown to improve (Gask et al., 2006).

The current focus on physical factors alone has not lead to significant reductions in T2D complications, since a medical model of treatment focuses primarily on adherence to medication. Adopting a more balanced approach and considering the psychological factors associated with T2D and its complications, may lead to an improvement in treatment outcomes. A longitudinal study investigating the predictors of depression in patients with T2D and peripheral neuropathy (PN) has established that, in patients with T2D, PN is linked to depressive symptoms and results in restrictions in activities of daily life and lower self-perceptions (Vileikyte et al., 2009; Vileikyte et al., 2005). This research also established that more severe levels of PN were associated with strong depressive symptoms, and that these worsened over time (Vileikyte et al., 2009; Vileikyte et al., 2005). There was also a strong link between an increase in depressive symptoms when combined with a decline in PN related physical and psychosocial functioning, indicating that, as PN increases its influence on other aspects of life, depression also increases (Vileikyte et al., 2009). This is directly relevant to patients with a DFU, as neuropathy is the direct precursor to DFU. The occurrence of a DFU is due to the underlying PN experienced by patients with T2D.

2.9 Identification & Treatment of Foot Ulcers

A DFU is a common complications of T2D. Standard care of a DFU is normally provided by a multidisciplinary team (Laing 1988). A multidisciplinary team is defined by the Australian Wound Management Association as “a number of people with complementary skills who are committed to a common purpose of health care provision and who work collaboratively with patients and their caregivers” (Moore et al., 2014 p. 59). A multidisciplinary team for the management of DFUs can vary slightly in its makeup depending on countries, resources and location, however, usually consists of disciplines such as a podiatrist, endocrinologist, nurse, vascular surgeon, orthotists, diabetologist or diabetes educator, and sometimes a radiologist or imaging specialist (Driver et al., Fabbi, Lavery, & Gibbons, 2010). Such a team ensures glycaemic control, adequate perfusion, local wound

care and regular debridement, off-loading of the foot, control of infection by appropriate antibiotics and management of comorbidities. The primary focus of the team is the medical management of the ulcer, and offloading or support of the foot, to continue to allow for some mobility considering the impact foot ulcers on individuals mobility. When a DFU does occur, there are many treatment approaches which may be employed in an attempt to heal the ulcer. The literature provides several different management approaches for treating DFUs, with the insight from reviewing this literature being there is no one single defined and accepted best practice.

When a wound is clean and debrided, ulcers heal faster (Pai & Madan, 2013). But devitalised necrotic tissue, common in DFUs adversely affect cell migration and lead to infection and delays of the healing process. Wounds heal faster when the dead necrotic tissue is removed, and bacterial load is reduced (Pai & Madan, 2013). The traditional way was to use a scalpel and remove all unwanted tissues including callus and eschar (sharp debridement). Necrotic tissue usually extends beyond the ulcer bed and hence, some authors recommend liberal debridement of deeper tissue beyond the ulcer boundary, thus increasing the ulcer size initially, to promote healing over time (Pai, 1996).

Wong, Leung and Wong (2001) reported 87% success rate in limb salvage by using repeated 'piecemeal' debridement's and herbal drinks. The radical debridement was said to cause inadvertent damage to the vascularity of local tissue. Another method propagated completely excising the chronic ulcer and the underlying bony prominences and converting it into a fresh ulcer. Some other researchers found good results with this approach (Armstrong et al., 2003; Piaggese et al., 1998). Inadvertent bleeding, poor pain tolerance by the patient and lack of any objective markers to differentiate impaired and healthy tissue to determine the extent of debridement are some of the limiting factors of sharp debridement (Pai & Madan, 2013). Physical debridement using wet-to-dry dressings, hydro-dissection or hydro-cision with the use of high pressure saline beam; enzymatic debridement using enzymes like

collagenase and papain as ointment preparations; autolytic debridement with the use of moisture retaining dressings and biological debridement with use of larvae of common green bottle fly are other methods of wound debridement. Essentially debridement is considered important to obtain healing, however by its very nature this leads to longer healing time as the ulcer is enlarged through debridement initially (Armstrong et al., 2003; Pai, 1996; Piaggese et al., 1998).

At times sharp debridement is joined with other forms of debridement to provide better healing. Saline-moistened gauze dressings are used to make wet-to-dry dressings, moisture retaining dressings made use of hydrogels, hydrocolloids, hydrofibres, transparent films and alginates. These materials provide physical as well as autolytic debridement. Antiseptic dressings are silver dressings and cadexomers. Researchers invented new ways of dressings, for instance, Vulnamin© gel made of amino acids and hyaluronic acid are used along with elastocompression and these have shown good results (Abbruzzese et al., 2009). Promogran© by Johnson and Johnson's is prepared by making a freeze dried matrix composed of collagen and oxidized regenerated cellulose (Thomas, 2002), while medicated honey is said to have anti inflammatory, antiseptic and osmotic properties, which can be used in dressings or in combination with sterile dressings to improve healing rates (Shukrimi, Sulaiman, Halim, & Azril, 2008). For offloading the foot Total Contact Cast (TCC), removable cast walkers, custom shoes, half-shoes, soft heel shoes, padded socks, shoe inserts, wheelchairs and crutches have been used. These are used to prevent and treat the DFU, by reducing the plantar pressure and redistributing it to a larger area, to avoid friction and to accommodate the deformities the above mentioned objects are used. The efficacy of a TCC, removable cast walker and half-shoe in patients with DFU were compared in a randomized control trial. The study found TCC to be the most effective modality (Armstrong et al., 2001). Compared with traditional dressings TCC as found to be the superior method in the treatment of plantar DFU (Mueller et al., 1989). The limiting factors for TCC include the requirement

of trained personnel for its application and expenses because of frequent cast changes. Removable cast walkers like Aircast walkers allow for monitoring of skin and dressing changes. Verity, Sochocki, Embil and Trepman (2008) found Aircast walkers to be more cost effective than TCC, however in comparison a recent systematic review, non-removable offloading devices (for example TCC) were more cost effective for ulcer healing than the removable off-loading devices such as Aircast walker, due to improved healing rates due to being irremovable by patients. (Morona, Buckley, Jones, Reddin, & Merlin, 2013). Once devices such as these, and specialist dressings are involved to improve the healing outcomes of DFUs, the cost for treatment increases, as does the complexity in managing these, both for the medical providers and also the patient.

2.10 Screening for Depression in People with T2D

A review of current T2D clinical care guidelines with respect to screening for depression includes a variety of recommendations. The International Diabetes Federation (IDF) states that healthcare professionals should, when communicating with a person with T2D, adopt a whole-person approach and respect the person's central role in their ongoing T2D education and care (IDF, 2005). There is no specific mention of management of psychological disorders or their impact on T2D management. Other national and international guidelines are more specific with respect to psychological disorders. By comparison, the British National Institute of Health and Clinical Excellence (NICE) states that:

“diabetes professionals should ensure they have appropriate skills in the detection and basic management of non-severe psychological disorders, while arranging prompt referral to specialists of those whom psychological difficulties continue to interfere significantly with their well-being or diabetes self-management” (NICE, 2004 p. 44). Once detected, it is recommended that:

“the psychological needs of people with diabetes should be addressed in an organised and planned way and that the individual’s psychological status (including cognitive dysfunction) should be assessed periodically, with outcomes and clinical implications discussed with the patient” (NICE, 2004 p. 44).

The American Diabetes Association (ADA) guidelines go slightly further, stating that “assessment of psychological and social situations should be included as an ongoing part of the medical management of diabetes” (ADA, 2014 p. 533). They specifically state that:

“psychosocial screening should examine attitudes about the illness, expectations of medical management and outcomes, affect and mood, general and diabetes-related quality of life, resources (financial, social and emotional) and psychiatric history...” (ADA, 2014 p. 533).

Screening should be provided for psychosocial problems such as depression, diabetes-related distress, anxiety, eating disorders and cognitive impairment, particularly when self-management is poor (ADA, 2014).

The Australian national evidence based guidelines for management of T2D briefly touches on the need for psychosocial management, (Diabetes Australia, 2016) yet in much less detail than the NICE or the ADA. The national evidence-based guidelines on prevention, identification, and management of foot complications in people with T2D, approved by the NHMRC in 2011 goes into extensive detail on the screening process for ‘at risk’ participants for DFUs and the evidence-based management of DFUs. This guideline however does not mention or refer to depression or depressive symptoms, and the effect this has on patients with or at risk of DFUs (Diabetes Australia, 2016). With the increasing literature linking T2D and mental health conditions, along with other international guidelines referencing the importance of considering the psychological needs amongst those with T2D, the Australian guidelines when referencing those at risk of a DFU could go further in providing guidance on managing depression or at least the importance of considering mental health conditions

amongst this population (Ali, Stone, Peters, Davies, & Khunti, 2006; Anderson, Freedland, Clouse, & Lustman, 2001; Carnethon et al., 2003; Lloyd et al., 2010; Pouwer et al., 2010).

In some quarters there is a reticence to discuss psychosocial factors with patients, due to the perceived emotional impact that raising such topics may have (Kalra, Jena & Yeravdekar 2018). The Australian health care system tends to focus on only the physical health or the mental health of a patient, and rarely both (Rutherford, Wright, Hussain, Colagiurii, & Australian Dawn Advisory Committee, 2004). Usually because those dealing with the physical symptoms don't realise these are linked to mental symptoms and are reluctant to address mental health issues. A systematic review and meta-analysis on the emotional impact of screening for disease found no evidence of any adverse emotional impact from undergoing a screening process, and reported that their findings are consistent with psychological theories of self-regulation through maintaining emotional equilibrium while managing threats (Carver & Scheier, 1982; Collins, Lopez, & Marteau, 2011). It was concluded that provided standard principals of screening were met, there was no adverse or long-term emotional impact when screening for a disease (Collins et al., 2011).

2.11 Measuring Depression in People with T2D

Regardless of the well-documented prevalence of depression in patients with T2D, there remains little emphasis on the psychological aspects of T2D in contemporary health care (Rutherford et al., 2004). The evidence linking a concurrent diagnosis of depression and T2D to an increased mortality, a lower level of self-care, and an increased risk of poor or even non-healing of DFU, should prompt treating clinicians to be more aware of a patient's ability to cope on a day-to-day basis with both their T2D and psychological malaise (Moore, 1997). When depression is stabilised, patients have been shown to be able to engage more readily in self-management activities, which will help improve their depression, T2D, and QoL (Schram, Baan, & Pouwer, 2009). Despite health care providers recognizing

psychological symptoms in many patients, only 10% in Australia are referred for psychological assessment or care (Rutherford et al., 2004).

A clinical diagnosis of a major depressive episode is made using a clinically structured interview and conducted by psychologists or psychiatrists based on the DSM-V criteria for depression. However, this process is very time consuming for both clinicians and participants (Sakakibara, Miller, Orenczuk & Wolfe, 2009). Moreover sub-clinical levels of depression can affect T2D prognosis, morbidity and mortality (Naicker et al., 2017). Therefore, health care providers could easily administer a psychometrically sound depression scale to screen for depression and refer patients to a psychologist or psychiatrists if necessary (McKellar, Humphreys, & Piette, 2004).

For this research, when considering the scale to be used to assess for and measure depressive symptoms amongst the population, three scales were compared: The Centre for Epidemiological Studies Depression (CES-D) scale; the Hospital Administered Depression Scale (HADS) and the Depression Anxiety Stress Scale (DASS). The CES-D has cut off scores that may be used to screen for depressed mood and provide discrete levels of depressive symptoms. This scale has also demonstrated excellent reliability with Cronbach's alpha of .85 and is the only one of the three scales with a good two-week test-retest reliability (Sakakibara, Miller, Orenczuk & Wolfe, 2009; Zhang et al., 2015). In comparison, both the HADS and the DASS use subscales to measure depression symptoms. The reliability and sensitivity of both these scales were lower compared to the CES-D (Sakakibara, Miller, Orenczuk & Wolfe, 2009). Also, when comparing these three scales, the CES-D and HADS both measured somatic symptoms. These were considered important in this research as QoL was also being investigated, and somatic symptoms are known to negatively influence QoL (Kapfhammer, 2006). However, compared to the HADS, the CES-D has been used more widely in previous diabetes research and was considered the best scale for this current research (Roy, Lloyd, Pouwer, Holt & Sartorius, 2012).

2.12 Quality of Life and Diabetic Foot Ulcers

An individual's QoL is their own perception of their health, comfort and happiness (World Health Organisation, 2004). The four aspects of an individual's life that are affected by the presence of a foot ulcer are: social, psychological, physical and economic health (Gilpin, & Lagan, 2008). These factors also form the domains of an individual's QoL. Many authors have established that in patients with a DFU, reduced mobility is a major contributing factor to impaired QoL. Adopting to a lifestyle change is also difficult for patients with a DFU (Ashford, McGee, & Kinmond, 2000; Brod, 1998; Ribu & Wahl, 2004).

Georgios et al. (2013) examined the health related QoL and diabetic neuropathy among T2D. The study was a quantitative one where patients were randomly chosen from two hospitals. The study found that health related QoL in people with T2D was poor. The study also stated that predictors for this poor QoL among individuals with T2D depended upon their activity level, blood sugar levels, mental fatigue, coronary artery disease, and depression. The implications of these findings are that such factors should be mitigated in patients who have T2D if QoL is to be improved along with treatment and health outcomes.

Doupis et al, (2008) examined the rates of DFUs in patients with lower extremity arterial disease. The authors stated that T2D can affect the QoL in patients and causes further economic burden to both the patients as well as the healthcare systems. The implications of this study are that diabetic ulcers when they occur can reduce the QoL of patients with T2D.

A review by Price (2004) assessed health rated QoL of people with T2D with foot complications. The main findings indicated that people with foot ulcers had a significantly poorer QoL than those who had experienced an amputation, as many individuals feared the recurrence of ulceration, infection and potentially life-long disability. This indicates that people with foot ulceration may need support to cope with any future complications that they may develop.

2.12.1 The Social Aspect

Numerous studies have indicated that people's daily, social and family life, as well as partaking in leisure activities, was affected when they presented with a diabetic foot ulcer (Ashford, McGee, & Kinmond, 2000; Brod, 1998; McPherson & Binning, 2002; Ribu & Wahl, 2004). In a pilot study by Brod (1998), all individuals with T2D and their caregivers reported an impaired QoL. This was due to reduced mobility experienced while adapting to a change of lifestyle that led to added pressure and burden on the individual's immediate family members and their caregivers, causing conflict and tension. It has been reported that people with T2D have a poorer QoL than people without chronic illness (Rubin & Peyrot, 1999). Diabetic foot ulcers are one of the major complications associated with T2D and have been shown to impact hugely on an individual's QoL (Rubin & Peyrot, 1999). Foot ulcers pose a major burden for many individuals. This may also include the family and friends of the person with T2D, as many assist in wound care and support the individual in coping with related physical and emotional suffering (Brod, 1998; Vileikyte, 2001).

A review examined the QoL of people with diabetic foot ulceration and reported that many depended on their family and friends to carry out tasks that they were not able to perform (e.g. dressing the ulcer and transporting to appointments) (Gilpin, & Lagan, 2008). This sometimes resulted in family relationship problems. All individuals reported that loss of mobility meant that they were unable to perform everyday tasks, such as shopping or bathing. Interestingly, as quoted by Gilpin and Lagan (p. 57, 2008) in their review of QoL aspects associated with DFUs "a recent phenomenological perspective study conducted by Watson-Miller (2006) revealed that people with a DFU did not report any social isolation. This is in contrast to other studies cited in this section which did note the problem of social isolation amongst this population (Kinmond, McGee, Gough, & Ashford, 2003; Ribu & Wahl, 2004). This may be due to the small sample size used by Watson-Miller (2006)". The above research reveals that the majority of people reported impaired QoL, particularly in their daily and

family life (Brod, 1998; Kinmond et al., 2003; Ribu & Wahl, 2004). Of notable interest was the Watson-Miller (2006) study that highlighted the importance of holistic assessment as a requirement in assessing people's QoL. The study also emphasised that healthcare professionals need to be aware of the difficulties that people who present with diabetic foot ulceration encounter.

2.12.2 The Psychological Aspect

Various studies have revealed that people who have a DFU also have many psychological and emotional effects. The major concern highlighted in the literature reviewed was that people's immobility led to various emotional symptoms (Brod, 1998; Kinmond et al., 2003; Watson-Miller, 2006). Brod (1998) noted that a significant number of individuals felt frustration, anger, and guilt resulting from restrictions that their DFU placed upon them. Depression was another symptom noted (Brod, 1998). However, positive aspects were reported including the development of closer relationships with the individual's partner or spouse, as they appreciated the support given to them (Brod, 1998). Caregivers often reported being angry and frustrated as the individual's illness was a life-long condition. However, the caregivers reported positive outcomes as they were made aware of the importance of foot ulcer prevention and had an awareness of the emotional needs of the person with the ulcer. Kinmond et al. (2003) conducted a phenomenological study approach using semi-structured interviews with people with T2D who presented with foot ulcers. The sample consisted of 6 females and 15 males and investigated the psychosocial aspects of QoL. Most of the participants reported negative effects on their social roles and activities because of their DFU. One individual reported that the immobility following 3.5 years of resting the affected foot ulcer, led to such unbearable depression that he begged for an amputation; however, this was not considered an option.

There is strong evidence suggesting that psychological distress and stress can disrupt the body's ability to heal wounds because they involve a biological process (Walburn et al.,

2009). Wound healing is a biological process, achieved through specific phases: haemostasis, inflammation, proliferation, and remodelling. For successful healing to occur, all four phases must occur sequentially and in a reasonable time frame. The disruption stress places on this process can be significant and can lead to healing delays: however, most research has focused on acute wounds and not chronic ones, such as DFUs (Vileikyte, 2007).

2.12.3 The Physical Aspect

Data from many small studies have revealed that foot ulcers have a significant impact on people's physical health, particularly in terms of reduced mobility as discussed above. Ashford, McGee, and Kinmond (2000) investigated the physical life of people with T2D who presented with foot ulceration through semi-structured interviews using a phenomenological approach. It was found that footwear was a major factor, in that many people disliked the type of shoes that they were required to wear. This study highlighted the females felt that their femininity was undermined by therapeutic footwear. However, this study assessed only a relatively small sample size and there was an uneven distribution between males ($N = 15$) and females ($N = 6$); therefore, the results may not be as accurate in suggesting that footwear is a real issue compared with those from larger scale studies. An earlier study emphasised the importance of footwear and noted that wearing protective shoes for more than 60 % of the time during the day can reduce the ulcer relapse rate by more than 50% compared with shorter wearing times (Chantelau & Haage, 1994). Reiber, Lipsky and Gibbons (1998) assessed the physical and mental function amongst a T2D population ($N = 302$) with a foot ulcer. They found that people with a foot ulcer had significantly lower physical and social function in all eight domains compared with those without an ulcer (Reiber, Lipsky, & Gibbons, 1998).

2.14 Depression and Diabetic Foot Ulcers

Gonzalez, Hardman, Boulton and Vileikyte (2011) stated that they believe the psychosocial aspects of foot ulceration is important and understudied, and further

understanding of the relationship between psychosocial conditions and ulcer outcomes is important.

The recent evidence of a substantial relationship between depression symptoms and DFU rates, with every standard deviation increase in depressive symptoms, associated with a 68% increase in risk of DFU, substantiates the need for further research in this area (Gonzalez et al., 2010). Ismail et al. (2007) more specifically investigated the association of depression with DFUs. The study employed a prospective cohort design and recruited 253 people. The study only recruited patients with their first DFU, and the main outcome measure was mortality. However, no information was obtained on healing rates of the ulcer. Depression was measured using a clinical assessment according to the DSM-IV criteria and diabetes was determined by HbA1C levels. Results were reported for both major and minor depressive symptoms. Major depression was found in 24.1% and minor depression in 8.1% of this sample. Higher levels of depression were associated with a threefold increase in mortality (Ismail et al., 2007).

Chapman, Shuttleworth, and Huber (2014) expressed the view that high levels of depression exists in patients with diabetic foot conditions. Their study however examined only patients with Charcot foot complications, and not those with a DFU. The authors concluded that depression was more severe and more common in people with a diabetic foot condition. This finding implies that depression is associated with the debilitating consequences of T2D and that depression must be given serious consideration of the impact it has on diabetic foot treatment. The findings by Ismail et al. (2007) and Doupis et al. (2008) also support and confirm an association between depression and diabetic foot complications, suggesting that it is imperative that those with a DFU should be screened for mental health conditions, in particular depression.

2.15 Research Gap and Theoretical Research Model

It is clear from the existing literature that has been reviewed that the health care costs and treatment techniques used in treating long-term neuropathic DFUs are significant (Davis, Norman, Bruce, & Davis, 2006; Driver et al., 2010; Kerr, 2012; NHMRC, 2005). It is also well established that there is a strong link between T2D and depressed mood, with depression in this population contributing to increases in morbidity and mortality (Ali et al., 2006; Anderson et al., 2001; DiMatteo et al., 2000; Katon & Ciechanowski, 2002; Lloyd et al., 2010; Pouwer et al., 2010). Despite the observed prevalence of depressive symptoms by health care professionals in Australia (Rutherford et al., 2004) and the recommendations of international guidelines that psychosocial symptoms need to be managed along with T2D care (ADA, 2014; NICE, 2004), depression remains under-recognized and undertreated in the DFU patient population. The complex interaction between depression and T2D has been established in people with PN (Vileikyte et al., 2009; Vileikyte et al., 2005); however, the addition of a DFU has further implications for the individual's capacity for self-care (Gask et al., 2006), and potentially increases the psychological impact of T2D. Lower levels of self-care and self-efficacy along with activity restriction are known to influence QoL (Ashford, McGee, & Kinmond, 2000). The relationship of different levels of depressive symptoms amongst a population with a DFU has on QoL requires further exploration, since lower QoL has a negative influence on management of T2D (Ashford, McGee, & Kinmond, 2000) and managing a DFU (Brod 1998). The notion that higher levels of depression will lead to longer healing time of a DFU is important when considering the impact treating a DFU has on both an individual through decreased QoL, and also the health care system, with increased costs.

The biopsychosocial model is a theory for understanding health and illness which proposes that changes in disease outcomes are multifaceted, and attributed to intricate relationships between biological, psychological and social factors (Borrell-Carrio, Suchman, & Epstein, 2004). King, (2008) stated that medical treatment is not complete without support

for psychological wellbeing. The biopsychosocial theoretical model is the approach that will be adopted in this study; considering the biological facets of T2D and time in days to heal a DFU; psychological facets of depression levels amongst a population with a DFU and social facets in measuring the QoL in a population with T2D and a DFU. As the relationship between depression and T2D is well established, and as Carnethon et al. (2003) found people with the highest levels of depression developed the highest levels of T2D over time. These relationships amongst a specific population with a DFU will also be explored in the current study. The relationships between each of the variables of healing time in days, QoL, depression and T2D levels will be investigated to determine the relationship each of these variables has with the overall healing time of a DFU. As any recommendations to improve the treatment of any one of these variables amongst this population should also consider the interactions and relationships between them.

2.16 Research Hypotheses

As evidenced above, the existence of depression in people with T2D and DFU is highly prevalent and reasonably well established. Yet there is a paucity of literature that has specifically investigated the relationship between depression and healing time of DFUs in people with T2D (Gonzalez et al., 2010). As stated in the introduction, the first aim of this study was to determine if there is a relationship that different levels of depressive symptoms have on the healing time of DFUs. It was hypothesised that people with higher levels of depressive symptoms, would take longer to heal their foot ulcer, when compared to those with lower levels of depressive symptoms.

The second aim as previously stated was to determine if there was a relationship between depressive symptoms, T2D and healing time of a DFU. Earlier intervention, diagnosis, and management of patients' depressive symptoms may have implications for improved management of T2D and therefore also DFU healing rates. Faster healing and lower levels of T2D have been shown to reduce health care costs, not only in patients with

PN, but for those with DFUs (Vileikyte et al., 2005). Amongst this population with a DFU, it was hypothesised that people with high levels of depressive symptoms also have high levels of T2D and longer DFU healing time. Further, it was hypothesised that there would be a mediating effect of T2D on the relationship between depressive symptoms and DFU healing time.

The third aim was to determine if there was a relationship between the mental health of patients with a DFU and individuals self-rated QoL, considering that previous research has indicated that depression has a negative influence on all aspects of QoL. Therefore, it was hypothesised that amongst the population with a DFU, higher levels of depressive symptoms would correlate with lower levels of QoL.

Chapter III: Methodology

3.1 Introduction

This chapter aims to present the methodological approach undertaken to determine the relationship between depression on quality of life and foot ulcer healing rates in T2D patients with a DFU. The sample selection, methodology employed, and data analysis is also outlined. Ethical issues associated with the study are then discussed

3.2 Research Purpose and Design

The study design adopted a descriptive research approach to discern if a relationship exists between depressive symptoms, QoL and ulcer healing rates in people with T2D. The research aims are outlined in Chapter 1 with the specific hypotheses aligning to the aims of this study are detailed in section 2.16. Both the aims and each of the specific hypotheses will be addressed throughout this study.

These will be investigated within a biopsychosocial framework as outlined in section 2.15. The findings of this research will be supported with data in answering the four hypotheses as outlined in section 2.16.

3.3 Study Population Sample

3.3.1 Sample

Data for this study was obtained from a single sample of individuals who were currently attending a High Risk Foot Service (HRFS) at Northern Health, Victoria, Australia for the treatment of a neuropathic DFU during 2013. Participants were drawn from all eligible and consenting patients admitted to the HRFS between January 1st 2013 to August 30th 2013. A total of 81 participants successfully recruited. This represents a 100% response rate of all eligible potential participants during the recruitment period. There were 59 males and 22 females, with a mean age of 62.6 years ($SD = 12.2$, range 21 years to 85 years). All participants had T2D, PN as assessed using a 10g monofilament (Nather et al., 2011) and a current DFU. Exclusion criteria included managing any influence that the treatment for depression or any mental health condition may have on the results. Therefore, any participant taking anti-depressant medication or seeking psychological treatment for depression or any other mental health condition during the recruitment period was excluded from this study. However, no participant was excluded on this basis. There were no dropouts or missing data during this study. No exclusions were applied on how the T2D was treated, as long as the patients remained within the HRFS and were not admitted to hospital or any other T2D service they remained eligible. There were no other exclusion criteria applied to ensure the broadest sample population of eligible participants was obtained for this study. Every participant of this study was an outpatient and remained an outpatient throughout the entire data collection period, therefore negating any possible influence of inpatient diabetes care that may exist had a participant been admitted to hospital during this study.

3.3.2 Sampling Technique

A simple random sample provides every participant with an equal opportunity to participate in the study. The researcher determined a research period of eligibility, and allowed every eligible participant the opportunity to partake. A simple random sample was drawn from a single site and all eligible participants were included. This determined the best possible results from the population and to minimise bias (Australian Bureau of Statistics, 1998).

3.4 Materials

3.4.1 Data Collection Instruments

Depressive symptoms: The Centre for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) is designed as a screening instrument for depression and is commonly used in primary medical clinics (Zich, Attkisson, & Greenfield, 1990). It is a reliable tool in measuring depression symptoms, and has shown good validity and sensitivity for diagnosing depression amongst the diabetic population (Haringsma et al., 2004; Zich et al., 1990). The CES-D is a 20-item scale, consisting of four possible responses to measure symptoms of depression across nine different areas according to the DSM 5th Edition (CESD-R, 2016). The four responses items are; ‘rarely or none of the time’, ‘some or a little of the time’, ‘occasionally or a moderate amount of time’ to ‘most or all of the time’ (Radloff, 1977). The symptom areas are; sadness (dysphoria), loss of interest (anhedonia), loss of appetite, sleep, thinking or concentration, guilt (worthlessness), tiredness (fatigue), movement (agitation) and suicidal ideation (CESD-R, 2016).

A review of the literature determined the cut off scores for different levels of depressive symptoms. A score of 0-16 is an indication of no clinical depression, scores of 16-

25 indicate mild depressive symptoms, while scores of 26 or greater indicate major depressive symptoms (Haringsma, Engels, Beekman, & Spinhoven, 2004; Zich et al., 1990).

The CES-D scale was also used to measure depression levels, as part of the Longitudinal Investigation of Depression Outcomes study in Australia along with the WHOQOL-BREF (Murphy et al., 2000). As this previous multicentre cross-national research had utilised both the CES-D and the WHOQOL-BREF, the QoL norms and depression cut off levels for the CES-D are well established. These questionnaires were thus determined to both be appropriate to measure depression levels and QoL amongst this sample population.

Quality of Life: The World Health Organisation's Quality of Life (WHOQOL) BREF 26 item (World Health Organisation, 2004) short questionnaire was used to assess individual's self-rating of their QoL. The WHOQOL BREF scale is available in 19 languages, other than English. This QoL scale has been validated for its ability to assess QoL in people with T2D and assess the relationship between QoL and HbA1C (Somappa, Venkatesha, & Prasad, 2014).

The WHOQOL BREF scale has an overall QoL rating, which has four individual domains that combine to produce the items of Overall QoL and Overall Health. Table 1 outlines each of the domains, and the 24 facets which each combine to comprise the four domains. The overall QoL calculated is a reflection across all domains for each participant.

Table 1

Domains and Facets of the WHOQOL BREF 26 Questionnaire (World Health Organisation, 2004)

Domain	Facet
Physical Health	1 Pain and Discomfort 2 Dependence on Medical Treatment 3 Energy and Fatigue 4 Mobility 5 Sleep and Rest 6 Activities of Daily Living 7 Work Capacity
Psychological Health	8 Positive Affect 9 Spirituality 10 Thinking, Learning, Memory and Concentration 11 Body Image and Appearance 12 Self-Esteem 13 Negative Affect
Social Relationships	14 Personal Relationships 15 Sexual Activity 16 Social Support
Environmental Health	17 Physical Safety and Security 18 Physical Environment 19 Financial Resources 20 Opportunities for Acquiring New Information 21 Participation in and Opportunities for Recreational/Leisure Activities 22 Home Environment 23 Health and Social Care 24 Transportation

Item range is 1-5. Each domain range is 0-100. Higher scores indicate better QoL. For each of the four domains, plus overall QoL and health, there are population norms. These population norms can be used to compare the study sample population to, and gain insights against a normal sample of the Australian population. No further details of participants socioeconomic level were investigated or obtained, as the participants in this study were

compared against these population norms for Australia. Table 2 presents the Australian population norms for the WHOQOL BREF scale as found by Hawthorne, et al., (2000).

Table 2

Australian Population Norms for the WHOQOL BREF Scale

Domain or Item	Mean	SD	Range
Item: Overall QoL	4.3	0.8	1.0 – 5.0
Overall Health	3.6	0.9	1.0 – 5.0
Domain:			
Physical Health	80.0	17.1	3.6 – 100.0
Psychological Health	72.6	14.2	20.8 – 100.0
Social Health	72.2	18.5	8.3 – 100.0
Environmental Health	74.8	13.7	28.0 – 100.0

Note :QoL = quality of life

Type 2 Diabetes: Levels of T2D were assessed from patients HbA1C, taken from their medical records. The HbA1C is a determination of an individual's glycated haemoglobin or plasma glucose concentration over a 3-month period. In T2D, higher amounts of glycated haemoglobin indicate poorer control of blood glucose levels or more severe levels of T2D. For this study the data will be analysed across three different levels of T2D using HbA1C levels. For the general population, a non-diabetic HbA1C is below 6mmol/L (NICE, 2004), while a well-managed blood glucose level in an individual with T2D is a HbA1C below 7.8mmol/L. A mild level of T2D was a HbA1C between 7.8mmol/L and 11mmol/L, with a

high level being over 11.1mmol/L. These cut-off ranges for a diabetic population, were guided by the NICE (2004) guidelines.

Each participant's HbA1C is measured upon their admission to the HRFS. For participants who were already in the HRFS prior to the commencement of this study, a current HbA1C was obtained at the time of the participant completing the questionnaires to ensure T2D levels were as accurate as possible. As such, data was not collected on the length of diagnosis of T2D for each participant.

Healing time: Each participant's length of active care in the HRFS, measured in days is the participants healing time. Each participant from their admission date has an episode of care, which is concluded upon discharge from the HRFS when healing of the DFU is achieved. During this study, some participants did not achieve complete healing during the data collection phase. The conclusion of the episode length was determined as at August 30th which is the end of the data collection period for this study. Each participants episode of care is counted backwards from admission, with a final treatment time if healing is not achieved prior, being August 30th, 2013.

3.5 Study Approach

Existing patients and all new patients who attended the Northern Health HRFS were screened for their eligibility by their treating podiatrists. Patients who met the eligibility criteria to participate in this research project were approached by the author. The author explained the study to the potential participant and provided them with the participant information and consent form (PICF). Participants who signed and returned the signature page of the PICF were included in the study. When participants attended their regularly planned appointment at the Northern Health HRFS, they were screened for levels of depressive symptoms by the main investigator, using the CES-D scale (Radloff, 1977).

The main outcome measures for this study were QoL and foot ulcer healing time. Participants were asked to complete the WHOQOL BREF, an unweighted valid psychometric instrument, during their attendance at the clinic. Participants with culturally and linguistically diverse backgrounds were provided with a copy of the WHOQOL BREF scale in their own language. At the same time for each participant, their current HbA1C was recorded from their medical record. Treatment time was calculated as number of days since admission to the service through to discharge date, which was documented once the DFU healed. The data was collated at the end of the data collection period for each participant, along with demographic information such as their age and sex taken from their individual medical file. Once the CES-D and WHOQOL questionnaires were completed by participants, each questionnaire was scored, with the results entered onto a database.

3.6 Ethical Considerations

Institutional ethics committee approval for this study was obtained from The Northern Health Ethics Committee, Melbourne, Australia. Ethics was duly followed in the research during all stages of the research along with ensuring to uphold the right of everyone who has participated such as rights to confidentiality and privacy.

3.7 Data Analysis

All data was analysed using SPSS version 20.0 (Chicago, IL, USA) (SPSS Inc., 2009). Values are shown as means \pm SD. A description correlation analysis is applied to the data. Before the analysis of the answers to the questionnaire, data cleaning was carried out to avoid any inconsistencies within the data. All questionnaires were completed in full, with no missing data identified in this study. Once sorted the data was coded and sorted to allow for statistical analysis.

The data was initially analysed using descriptive statistics, and correlations to explore relationships. The analysis strategy then used a predictive general linear model approach to investigate the relationships between the dependant variable (DV) healing time on the predictors (independent variable, IV), QoL, T2D level and depression levels. R^2 is the coefficient of determination, which means the proportion of the variance in the dependent variable that is predictable from the independent variable, and was calculated for significant effects. The relationship between depression, T2D, QoL and healing time was also investigated for a mediation effect by T2D. Multiple mediation with bootstrapping using a Preacher and Hays (2008) approach was performed for total and specific effects of the DV on the IV through the mediator of T2D on healing time. Effect size measures complemented all inferential tests, along with their associated 95% confidence intervals.

Chapter IV: Results

4.1 Introduction

The results are presented in mean $\pm SD$ and percentages, with the p -value $< .05$ considered as significant.

4.2 Descriptive Results

The descriptive statistics of the sample population for depression measured by the CES-D, T2D level measured by HbA1C, and healing time in days are presented in Table 3.

Table 3

Descriptive Statistics for Study Variables (N = 81)

Variables	$M \pm SD$	Median	Range (Min-Max)
Depression	19.6 ± 11.6	19.0	(0-44)
T2D	8.9 ± 2.9	8.2	(5.0-21.4)
Healing Time	290.4 ± 283.2	191.0	(11-1156)

Note: T2D = type 2 diabetes

The prevalence of depressive symptoms in this population, using the cut off scores as defined by Zich, Attkisson and Greenfield, (1990) for major, mild and no clinical depression, found that 58% had some depressive symptoms. Twenty-eight (34.6%) participants had major depressive symptoms and 19 (23.4%) participants had mild depressive symptoms, and 34 (42%) participants had no clinical depressive symptoms.

The frequency of the sample population for each of the three levels of T2D are presented in Table 4.

Table 4

Frequency of T2D Levels derived from HbA1C, taken from Patient's Medical Records

T2D Level	<i>N</i> (%)
Well managed (<7.8 mmol/L ^a)	30 (37.0)
Mild (7.8-11.0 mmol/L ^a)	35 (43.2)
High (≥ 11.1 mmol/L ^a)	16 (19.8)
Total	81 (100.0)

Note: ^aCut off levels as per NICE (2004); T2D = type 2 diabetes

To explore the primary aim of determining if there is a relationship between different levels of depressive symptoms and the healing time of DFUs, the descriptive statistics for the population were calculated across the three levels of depressive symptoms. Table 5 presents the healing time which was observed to increase from less days amongst those with no depressive symptoms to almost 3.5 times longer amongst those with major levels of depressive symptoms. This result confirms the first hypothesis; that people with higher levels of depressive symptoms take longer to heal a DFU when compared to those with lower levels of depressive symptoms.

Table 5

Descriptive Statistics and Confidence Interval for Levels of Depressive Symptoms on Healing

Time (Days)

Dependent Variable	Depressive Symptoms	<i>N</i>	Mean	<i>SE</i>	95% Confidence Interval	
					Lower Bound	Upper Bound
Healing Time	No Clinical Depression (0-15)	34	154.88	48.84	57.53	252.22
	Mild Depressive Symptoms (16-26)	19	262.80	64.16	134.94	390.67
	Major Depressive Symptoms (> 26)	28	536.04	70.15	396.22	675.85

Table 6 displays the Pearson correlations for depressive symptoms against T2D, healing time and the QoL subscales. A strong positive relationship was observed between depressive symptoms and T2D. A moderate correlation was observed between depressive symptoms and healing time. This significant correlation supports the second hypothesis that people with high levels of depressive symptoms would have higher levels of T2D. This also confirms the first hypothesis that people with higher levels of depressive symptoms take longer to heal a DFU when compared to those with lower levels of depressive symptoms.

Depressive symptoms were found to have a strong negative relationship with overall QoL and overall health, and moderately strong negative relationship with the domains of physical health, psychological health, social relationships, and environmental health. The negative correlations indicate that as depressive symptoms increase, there is an associated negative impact on people's overall QoL. That is their overall health, physical health, psychological health, social relationships, and environmental health. All the correlations for depressive symptoms were statistically significant. These results support the third hypothesis that amongst people with T2D and a DFU, higher levels of depressive symptoms would correlate with lower levels of QoL.

Table 6

Pearson Correlations of Depressive Symptoms with T2D, Healing Time and QoL

Variables	<i>r</i>
T2D	.624
Healing Time	.483
Overall QoL	-.656
Overall Health	-.715
Physical Health	-.579
Psychological Health	-.590
Social Relationships	-.537
Environmental Health	-.513

Note: T2D = type 2 diabetes; QoL= quality of life; all $p < .01$

The Pearson correlations for T2D against healing time and the QoL subscales are presented in Table 7. There was no significant correlation between levels of T2D and healing time, indicating that there was no direct relationship between T2D levels and the healing time of a DFU. Type 2 diabetes levels had a moderately negative relationship with overall QoL, physical and psychological health, social relationships, and environmental health. A stronger negative relationship was found between T2D and overall health. These negative correlations indicate that as levels of T2D increase, there is an associated negative impact on people's health and all aspects of their QoL.

Table 7

Pearson Correlations of T2D with Healing Time and QoL

Variable	<i>r</i>
Healing Time	.139
Overall QoL	-.382**
Overall Health	-.561**
Physical Health	-.356**
Psychological Health	-.352**
Social Relationships	-.238*
Environmental Health	-.371**

Note: T2D = type 2 diabetes; QoL= quality of life; ** $p < .01$, * $p < .05$

Following from the correlations for T2D, and to explore the second aim of determining the relationship between levels of depression, T2D and healing time; Table 8 displays the combined effects across each of the three levels of both T2D and levels of depression and healing time. The longest mean time to heal a DFU was in participants with the lowest level of T2D and the highest level of depressive symptoms. It was also observed that amongst participants with no depressive symptoms, those with well managed levels of T2D had a mean healing time longer than those with mild levels of T2D.

Table 8

Descriptive Statistics and Confidence Intervals for Combined Effects of Depression and T2D on Healing Time (Days)

Dependent Variable	Depression	T2D	N	Mean	SE	95% Confidence Interval	
						Lower Bound	Upper Bound
Healing Time	No Clinical Depression (0-15)	Well managed	24	181.75	52.98	76.17	287.33
		Mild	10	128.00	82.07	-35.57	291.57
		High	0	0.00 ^a	0.00	0.00	0.00
	Mild Depressive Symptoms (16-26)	Well managed	4	240.00	129.76	-18.62	498.62
		Mild	10	298.60	82.07	135.03	462.17
		High	5	249.80	116.06	18.48	481.12
	Major Depressive Symptoms (>26)	Well managed	3	751.50	183.51	385.75	1117.24
		Mild	14	439.33	67.01	305.78	572.88
		High	11	417.27	78.25	261.32	573.23

Note: ^a This level combination of factors is not observed; T2D = type 2 diabetes; QoL = quality of life

Table 9 presents the descriptive statistics for each level of T2D on both QoL and healing time. The mean overall QoL across each level of T2D was found to be consistent, with a slightly higher mean QoL found for participants with the highest levels of T2D followed by participants with well managed and then mild levels of T2D. Healing time across the three different levels of T2D from this sample population were found to be varied. The highest mean healing time was observed amongst the population with a well-managed level of blood sugar, while the lowest mean healing time was found amongst the participants with mild levels of T2D.

Table 9

Descriptive Statistics and Confidence Interval for T2D on QoL and Healing Time (Days)

Dependent Variable	T2D	Mean	SE	95% Confidence Interval	
				Lower Bound	Upper Bound
Overall QoL	Well managed	3.22	0.22	2.77	3.67
	Mild	3.18	0.13	2.92	3.44
	High	3.27	0.20	2.86	3.68
Healing time	Well managed	391.08	76.97	237.68	544.49
	Mild	288.64	44.67	199.61	377.68
	High	333.54	69.99	194.05	473.02

Note: T2D = type 2 diabetes; QoL= quality of life

To further investigate the relationships amongst the three levels of depressive symptoms; no depression, mild and major depression, and the three levels of T2D within the sample population; well managed, mild and high, on QoL and healing time, a 3 x 3 analysis of variance was performed. The results are shown in Table 10. A significant effect with large effect size was found for depressive symptoms on QoL, $F(2,77) = 17.06$, $p < .001$, $\eta^2 = .319$. A significant effect also with large effect size was also found for depressive symptoms on healing time $F(2,77) = 8.89$, $p < .001$, $\eta^2 = .196$. There were no significant effects found for T2D on either QoL or healing time.

Table 10

ANOVA of the Relationship Between All Depression Levels and All T2D Levels on QoL and Healing Time (Days)

Source	DV	Sum of Squares	df	Mean Square	F	p	η^2
T2D	Overall QoL	1.62	2	0.81	1.40	.252	.037
	Healing time	118253.05	2	59126.53	0.88	.420	.023
Depression	Overall QoL	19.75	2	9.87	17.06	<.001**	.319
	Healing Time	1198249.91	2	599124.95	8.89	<.001**	.196
T2D x Depression	Overall QoL	2.10	3	0.70	1.21	.312	.047
	Healing Time	155705.39	3	51901.79	0.77	.514	.031

Note: R Squared = .442; Adjusted R Squared = .234 Computed using alpha =.05; ** $p < .01$, * $p < .05$; T2D = type 2 diabetes; QoL = quality of life; ANOVA = analysis of variance

A Preacher and Hayes (2008) conditional process analysis was conducted using a mediation model with bootstrapping to better determine the mediating role of levels of T2D on the relationship between depression and healing time. Consistent with earlier analysis, Table 11 displays the finding of a significant association of depression on healing time ($TE = 171.19$, $SE = 41.35$, $p < .01$). A partial mediation effect was found for T2D on the relationship between depression and healing time ($TE = -28.51$, $SE = 27.62$, $p < .01$). This supports the third hypothesis that there is a mediating effect of T2D on the relationship between depression and healing time.

Table 11

Mediation Effects of T2D on the Relationship of Depression and Healing Time (Days)

					95% Confidence Interval	
Depression on					Lower	Upper
Healing Time	<i>TE</i>	<i>SE</i>	<i>t</i>	<i>p</i>	Bound	Bound
Total Effect	142.69	32.59	4.38	.001**	77.83	207.56
Direct Effect	171.19	41.35	4.14	.001**	88.87	253.52
Indirect Effect	-28.51	27.62		.001**	23.72	85.99

Note: *TE* = Total Effect; T2D = type 2 diabetes; ** $p < .01$

To determine the amount of influence T2D has on healing time, effect size was calculated. Table 12 presents the mediation effect was of medium size, with T2D explaining 21% of the relationship between depression and healing time ($R^2 = 0.208$, $p < .001$).

Table 12

T2D Mediation Effect Size for the Relationship of Depression and Healing Time (Days)

						95% Confidence Interval	
<i>R</i> -						Lower	Upper
	Coefficient	<i>SE</i>	Squared	<i>t</i>	<i>p</i>	Bound	Bound
Constant	60.98	79.90		0.76	.448	-98.09	220.05
T2D	-54.91	49.14	0.208	-1.12	.267	-152.74	42.93
Depression	171.19	41.35		4.14	.001**	88.87	253.52

Note: T2D = type 2 diabetes; ** $p < .01$

To explore the third aim to determine the relationship depressive symptoms have on individuals self-rated QoL in people with a DFU. Table 13 displays the descriptive statistics for overall QoL across all levels, for the combined effects of depressive symptoms and T2D. The lowest QoL was observed amongst the participants with major levels of depressive symptoms and well managed T2D. The highest mean level of QoL was found in participants with mild depression and high levels of T2D followed by the participants with no depression and well managed levels of T2D.

Table 13

Descriptive Statistics and Confidence Intervals for Combined Relationship of Depression and T2D on QoL

Dependent Variable	Depression	T2D	Mean	SE	95% Confidence Interval	
					Lower Bound	Upper Bound
Overall QoL	No Clinical Depression (0-15)	Well managed	3.92	0.15	3.61	4.22
		Mild	3.80	0.24	3.32	4.28
		High	0.00 ^a	0.00	0.00	0.00
	Mild Depressive Symptoms (16-26)	Well managed	3.75	0.38	2.99	4.51
		Mild	3.20	0.24	2.72	3.68
		High	4.00	0.34	3.32	4.68
	Major Depressive Symptoms (>26)	Well managed	2.00	0.54	0.92	3.07
		Mild	2.53	0.19	2.14	2.92
		High	2.54	0.23	2.09	3.00

Note: ^a This level combination of factors is not observed; T2D = type 2 diabetes' QoL = quality of life

To understand the relationship of different levels of depressive symptoms, have on the QoL for this population, the descriptive statistics are presented in Table 14. Overall QoL was

found to be lowest in the participants with major depressive symptoms. The highest QoL was observed in the group with no depressive symptoms.

Table 14

Descriptive Statistics and Confidence Interval for Levels of Depressive Symptoms on QoL

Dependent Variable	Depression		Mean	SE	95% Confidence Interval	
					Lower Bound	Upper Bound
Overall QoL	No Clinical Depression	(0-15)	3.86	0.14	3.57	4.14
	Mild Depressive Symptoms	(16-26)	3.65	0.19	3.27	4.02
	Major Depressive Symptoms (> 26)		2.36	0.21	1.95	2.77

Note: QoL = quality of life

Table 15 presents the descriptive statistics for the QoL variables from this study population and compares these against the statistics established from a normal Australian population in the study conducted by Murphy et al., (2000). This comparison for overall QoL and health of the sample against the established norms of the Australian population clearly indicate this sample has a significantly lower mean; $F(1,10) = 5.77, p < .05$. It is clear for the four domains that in this sample, the mean and SD are considerably lower when compared to the norms for Australia. The Australian range of scores for the four domains was also much broader, with all four norms including scores at the maximum level, compared to the maximum recorded score for the sample for all domains below 50% of the possible score.

Table 15

Comparison of Study QoL with Australian Population Norm QoL (Murphy et al., 2000)

Variables	Sample Mean $\pm SD$	Norm Mean $\pm SD$	Sample Range Min-Max	Norm Range Min-Max
Overall QoL	3.32 \pm 0.97	4.30 \pm 0.80	1-5	1-5
Overall Health	3.01 \pm 1.04	3.6 \pm 0.90	1-5	1-5
Physical Health	21.74 \pm 3.99	80.0 \pm 17.10	13-30	4-100
Psychological Health	18.58 \pm 4.39	72.6 \pm 14.20	8-26	21-100
Social Relationships	8.86 \pm 3.01	72.2 \pm 18.50	3-15	8-100
Environmental Health	27.53 \pm 6.62	74.8 \pm 13.70	15-40	25-100

Note: QoL = quality of life; Overall Health range is 1-5, Domain range is 0-100. Higher scores indicate better QoL

Chapter V: Discussion

According to the latest estimates from the WHO, 5.9% of the Australian population experience depressive symptoms, which is consistent with other countries, such as the United States (5.9%) (World Health Organisation, 2017). With previous studies consistently finding the prevalence of depression in people with T2D is approximately 2-3 times higher than the general population, the frequency of depressive symptoms expected amongst this sample was to be consistent with those found in prior studies of depression and T2D (Ali, Stone, Peters, Davies, & Khunti, 2006; Anderson, Freedland, Clouse, & Lustman, 2001; Lloyd et al., 2010; Pouwer et al., 2010). The sample population was from a single High Risk Foot Service located on the urban fringe of Melbourne, Australia. There is no other service for managing DFUs, and this clinic has a large catchment area which includes suburbs with high grown rates. The participants can be considered representative of the general Australian population with Australian census data indicating consistency across several dimensions including income and education (Australian Bureau of Statistics, 2018). However, the frequency of depressive symptoms observed in this study was found to be 10 times more prevalent, at 58%. This study demonstrates that consistent with prior studies, the rates of depressive symptoms amongst people with T2D is higher than the general population. However, when individuals also have a DFU, the frequency of depressive symptoms is higher again. This frequency of depressive symptoms compares well with the results found previously by Ismail et al., (2007) who found that 32% of their patients with T2D and a DFU had either minor or major depression. The prevalence of depressive symptoms amongst the DFU population indicate there is a need to address mental health conditions; particularly depressive symptoms when developing an effective DFU treatment plan.

5.1 Relationship between depressive symptoms and healing time

It was expected that in any sample of people with T2D, not every participant would have depression symptoms. And thus, comparisons and analysis on healing rates and QoL could be made between participants with none, moderate and major depressive symptoms. The results support the first hypothesis that there would be a relationship between depressive symptoms and healing time. The healing time for those with major depressive symptoms was more than double that for mild depressive symptoms, and almost 3.5 times longer than participants with none to low depressive symptoms. This considerable difference has a real-world impact. A recent systematic review by Chan et al. (2017) has found that the mean one-year public health cost per DFU was \$44,200. With depression having a relationship with the healing time of DFUs, the impact of lowering an individual's level of depressive symptoms even from major to mild is potentially significant and can have a positive impact on both the time to heal a DFU, and therefore also the cost of DFU treatment. Depressive symptoms have been found to influence individual's ability to self-care, as well as lead to reduced energy, appetite, and motivation (Lloyd et al., 2010; Vickers et al., 2006). Nutrition is important for healing, as is motivation and aspects of self-care to comply with optimal treatment to ensure timely healing of DFUs (Moore et al., 2014). Therefore, changes in any of these can lead to increased healing time, and with research demonstrating the influence depressive symptoms have on these factors, a deterioration of any of these elements may lead to increased healing time (Ford & Erlinger, 2004; Lloyd et al., 2010; Vickers et al., 2006). The focus on treatment of a DFU by engaging patients to be more compliant with the control of their T2D (Gask et al., 2006), and utilization of timely specialist treatments as identified by Tan et al. (2011) has improved treatment outcomes. Research by Prompers et al. (2008) on improving PAD as well as controlling infection (van Battum et al., 2011), along with the priority when treating a DFU to improve T2D levels are all considered central to achieving fast ulcer healing and

ideal treatment outcomes. The potential for improved integration of mental health specialists into the multidisciplinary treatment of patients with a DFU could assist in negotiating the balance between the medical and psychological model of treatment.

5.2 Relationship between depressive symptoms, T2D and healing time

The second hypothesis that those participants with higher levels of depressive symptoms would also have higher levels of T2D and longer healing time was supported. The strong correlation observed between depressive symptoms and levels of T2D, consistent with findings of previous studies that found the same association (Black, 1999; Carnethon et al., 2003; Ismail, 2009; Leedom, Feldman, Procci, & Zeidler, 1991; Lloyd, Matthews, Wing & Orchard, 1992; Musselman, Betan, Larsen, & Phillips, 2003; Padgett, 1993). Specifically, where participants who had high levels of T2D also were observed to have the highest levels of depressive symptoms (Carnethon et al., 2003). However, as no previous research has investigated the relationship between all three variables of T2D, depressive symptoms and healing time these findings cannot be directly compared or supported by prior studies.

None of the other correlations for T2D were as strong as the correlations found with depression. Interestingly, no significant correlation was found between T2D and healing time, indicating that as T2D levels increase there is no associated increase in the healing time of DFUs. The findings of Rerkasem et al. (2008) and Ortegon, Redekop and Niessen (2004) found that improvements in the management of T2D improved DFU complications and outcomes however these studies did not specifically look at healing time of the DFUs. The results from this study indicate that T2D levels alone do not appear to have an association with DFU healing time.

5.3 Relationship between depressive symptoms and Quality of Life

The third hypothesis that higher levels of depressive symptoms would correlate with lower levels of QoL was supported. In this sample, the strongest negative correlation was found between depressive symptoms and the combined QoL measure of overall health, closely followed by overall QoL. With a significant correlation observed for each of the four QoL domains individually, it follows that the strongest correlations would be observed in the two overall measures which combine the four domains. With overall health having the strongest negative relationship with depressive symptoms, these findings support the overwhelming evidence base that higher levels of depression and associated symptoms leads to lower levels of health and also QoL (Georgios et al., 2013; Price, 2004; Rubin & Pyrot, 1999). The strong correlations of depressive symptoms with all QoL variables highlight this relationship among people with T2D and an active DFU. In this sample, the QoL subscale psychological health demonstrated the individual domain which had the strongest negative relationship with depressive symptoms closely followed by physical health. This finding aligns with prior research and underlines the relationship psychological health has with depressive symptoms amongst a population with T2D and a DFU (Brod, 1998; Kinmond et al., 2003; Watson-Miller, 2006).

Quality of life is often overlooked in clinical practice (Brown, et al., 2000). The primary focus of treatment is to only focus on treating the DFU and the T2D, while assuming that an individual's QoL will subsequently also improve (Piaggese, et al., 1998). However, psychosocial factors are not so readily considered. For chronic conditions such as DFUs, a review of the published literature identified that the link between QoL and how it can influence T2D complications such as DFU has not previously been considered. This is an area where further investigation should be focused. This study found that T2D was negatively correlated with QoL. The strongest negative correlation was observed for overall health,

indicating that an increase in T2D level has a strong negative relationship with individual's overall health rating. This finding matches those of earlier studies and the widely accepted understanding that T2D negatively impacts on health and QoL (Ashford et al., 2000; Brod, 1998; McPherson & Binning, 2002; Ribu & Wahl, 2004; Vileikyte et al., 2005). The strength of all the correlations between T2D and QoL domains, were less when compared with those between depression and QoL, however all were significant.

5.4 Relationship between T2D and DFU healing time

When the effects of both depressive symptoms and T2D were combined, the descriptive data reflects the findings for the relationship between depression alone and healing time. Higher levels of combined depression and T2D were associated with longer healing times. The longest time to heal a DFU was in participants with well managed levels of T2D and the highest level of depressive symptoms. The mean time taken to heal a DFU for this combination was more than 1.7 times longer than the next longest combination. With further scrutiny, this result appears to be skewed by the small number of participants (3) in this grouping. The results for healing time across each of the three T2D levels, should therefore be interpreted with caution as subsample sizes were quite small.

The correlation found between T2D and healing time was not significant, however there was a strong correlation between depression and healing time. This finding supports prior research, which identified the negative impact depressive symptoms have on an individual's self-care, and that individuals with depressive symptoms may be less likely to follow clinical advice and generally have higher levels of obesity (Golden et al., 2004, 2007; Lloyd et al., 2010; Marcus, Wing, Guare, Blair, & Jawad, 1992). This combined effect of both depressive symptoms and T2D also further confirms the relationship finding between T2D and healing time, and indicates that T2D levels may not have any influence on the time to heal a DFU if depressive symptoms are present. Further research should be conducted to

replicate and confirm these findings, as well as explore the influence that an individual's self-efficacy has on the healing time of DFUs.

The shortest time to heal a DFU was found in the participants with no depressive symptoms and mild levels of T2D. At the outset as it was hypothesised, participants with higher levels of depressive symptoms would have higher levels of T2D and longer healing time. However, as the results of this study indicate, T2D levels alone appear to have no influence on DFU healing time. With this knowledge, it could be expected that participants with no depressive symptoms and both well managed and mild levels of T2D would have similar and the lowest healing times. The interesting finding that mild levels of T2D had a lower healing time is similarly due to the same reason for the longest healing; that is impacted by the small number of participants with this particular time to heal combination. Only 10 participants had both no depression and mild T2D, compared to 24 with the combination of no depression, and normal levels of T2D.

To further understand the relationship of T2D on healing time, a mediation model was conducted. It was found that levels of depressive symptoms have a direct and significant relationship on healing time, and that T2D only partially mediates this relationship. The third hypothesis that there would be a mediating effect of T2D on the relationship between depressive symptoms and healing time is partially supported, as there is an indirect effect of 21% and the mediation effect observed is negative. These results indicate that there is some influence of T2D on the relationship, however as this mediation is only partial, it is likely that there are other influencing factors as well as T2D, which have not been considered in this study. This would confirm the findings established by Barnard et al., (2012), that it is important to consider the other influences that may negatively impact on DFU healing, and not just T2D levels. Other influences may include infection of the ulcer, treatment methodologies, PVD and associated T2D complications (Barnard et al., 2012).

There are currently no other studies available examining the relationship of depressive symptoms, T2D and DFU healing time which would allow direct comparisons with these findings. With the small numbers of participants in each group, these findings do not directly contrast those of previous research; namely that higher levels of T2D lead to an increased number of DFUs and associated diabetic complications (Alberti et al., 2004; Charnogursky, Lee & Lopez 2014) however neither of these specifically investigated DFU healing time.

5.5 Ability to self-care influence on T2D levels and healing time

The concept of self-efficacy is important for self-management behaviours for individuals with T2D (Lloyd et al., 2010; Vickers et al., 2006). Self-efficacy is defined by Bandura (1977) as an individual's belief in their own capacity to perform certain behaviours necessary to achieve outcomes, such as self-control, motivation and achieving set tasks. Research has found that an individual's ability to comply with treatment directions, instructions, medical adherence and appropriate preventative care for their T2D, such as dietary regimes and exercise is diminished when higher levels of depression are present (Lin et al., 2004). This concept of diminished self-efficacy impacting on an individual's management of their condition is supported by a controlled trial confirming the hypothesis that people with depression were more likely to engage in behaviour known to increase the risk of developing T2D, and that people who had T2D complications were more likely to develop depression (Katon et al., 2004).

5.6 Quality of Life across different levels of T2D

There was very little difference in overall QoL across the three levels of T2D, while overall QoL decreased as depressive symptoms increased, reflecting the correlation revealed earlier. When the three levels of both depression and T2D were combined, a significant correlation was only found for depression with QoL, with a large effect size. These findings

align with those of previous research and the accepted understanding that depressive symptoms have a negative association with an individual's self-rated health amongst the diabetic population (Brod, 1998; Kinmond et al., 2003; Watson-Miller, 2006).

Individuals QoL can be influenced by many variables. This study demonstrated that of this population, overall QoL did vary across different levels of T2D and depression.. Due to the small numbers it cannot be concluded that T2D did not influence overall QoL amongst those most depressed, particularly as there was a negative relationship between T2D and overall QoL.

When comparing the Overall Health and QoL of this sample against a population of Australians without T2D (Hawthorn et al., 2000), it is clear the influence that chronic disease has. Across the four domains of physical and psychological health, social relationships, and environmental health, the difference between mean scores is considerable, with this study sample found to have mean quality ratings over 60% lower when compared to Australian population norms (Hawthorn et al., 2000). It is worth noting that not one score for the sample was over 50 from a possible maximum domain score of 100.

The lowest QoL domain score identified amongst the sample was social health, which includes the facets of personal relationships, social support, and sexual activity. These results demonstrate that participants who have a DFU and depression reported the most social isolation and had the lowest self-rated personal relationships. These results confirm those of prior studies, that individuals daily, social and family life as well as partaking in social or leisure activities were impacted due to the presence of a DFU (Ashford, McGee, & Kinmond, 2000; Brod, 1998; McPherson & Binning, 2002; Ribu & Wahl, 2004). When compared to the normative data of the Australian population, social health was also the lowest domain of the four (World Health Organisation, 2004). Compared to the other domains of psychological, physical, and environmental health, Australians self-rate social health lowest. Considering

this, and the prior research, the findings observed in this study are consistent in the order of the domains with the Australian population norms, just at a much lower mean level for each domain. This is an important consideration when treating a patient with a DFU. Since social health encompasses social support and personal relationships, both which are so important in effectively managing a DFU, having low levels of this as found in these results, has a and negative impact on healing time (Brod, 1998; Kinmond et al., 2003; Ribu & Wahl, 2004).

Psychological health was the second lowest average domain, including facets of self-esteem, body image, thinking, learning, memory and concentration (World Health Organisation, 2004). These results match those of the Australian population, who also rated psychological health second lowest (World Health Organisation, 2004). Understandably these are negatively impacted when an individual has a DFU, with previous studies highlighting the psychological influence of DFUs on psychological health (Brod, 1998; Kinmond et al., 2003; Watson-Miller, 2006).

Understanding the relationship that T2D, depression and high blood sugar have on individual facets of QoL, as well as the broader domains that make up overall QoL may provide those who treat these patients with alternative focus areas where a greater impact of treatment can be made. Considering from this population that participants experienced poor thinking, self-esteem, social support, mobility and body image amongst many other facets, there is a clear opportunity to enhance treatment outcomes by increasing the importance of addressing these psychological factors more directly. Especially considering that a relationship was found between the three variables of depression, DFU healing time and participants QoL.

5.7 Methodological Limitations of the Study

There were several limitations to the methodology of this study. The short timeframe when data could be collected is one limitation, which may influence the number of

participants recruited, as well as the range of symptoms within this population. All participants were attending a HRFS located in one particular metropolitan location of Melbourne, which may narrow the socioeconomic population the sample was drawn upon, and possibly not including a broad divergence across all socioeconomic levels. There were also some limitations discovered after the analysis of the sample. Where splitting out the sample to investigate the influence of combined effects of depressive symptoms and T2D, this in some particular combinations adversely diluted the sample size, which lead to skewing some means and giving the perception of some combinations having greater influences than they possibly may if a larger sample with more even spread was obtained.

Participants who were existing patients of the HRFS, prior to the start of the data collection were included. Due to the extended length of ulcer treatment time, some participants may have had received previous mental health treatment, which had ceased prior to the commencement of this study. The exclusion criteria only excluded any participants currently receiving medication or treatment for depression during the data collection period.

There are also some limitations around obtaining accurate HbA1C data. The variability around when this test was undertaken following admission, may lead to some error in accurately determining each participant's level of T2D. It was determined that the HbA1C be used instead of an average of daily blood glucose levels, since the HbA1C is a 3-month average, so provides the best long-term indication of blood glucose level. The method also did not indicate which participants were well managed with their T2D, and those who were not, or if the management of their T2D was with medications, diet or unmanaged.

Throughout this research, it was assumed that all participants adhered and complied with best treatment, however as previous research has established, an individual's self-efficacy is influenced by depressive symptoms (Lloyd et al., 2010; Vickers et al., 2006). There was no control during this study to ensure that individual participants did follow their

prescribed best treatment to ensure optimal DFU healing time. This is an area where further research could be undertaken to better understand amongst the DFU population, the influence depression has on individual's adherence with treatment and their own self-care.

There are some limitations in the analysis of the data and the groupings of both depressive levels and T2D levels. These groupings and cut-off levels, defined in the method section and used in the analysis, in some cases resulted in very small group sample sizes. This has consequences for the ability to draw conclusions.

In conducting this study into the relationships between depression, QoL and T2D there are some limitations in the statistical analysis predominantly used. Correlational analysis allows for determining relationships between variables, and also the direction of the relationship, however this analysis approach is unable to determine causality between the variables. As this study was investigating the relationship between the variables, causality was not the aim, and therefore this limitation is acknowledged. Future research following from this study may include an explanatory research approach or randomised control trial to extend these correlational findings and further understand the causation of these now established relationships.

Chapter VI: Conclusions

The conclusion of this study is that that a relationship has been established between depression, QoL and DFU healing rates in people with T2D.

The first aim of this research was achieved through the finding that there is a relationship between depressive symptoms and the healing time of DFUs. To investigate this aim, the first hypothesis, that people with high levels of depressive symptoms will take longer to heal, when compared to those with lower levels of depressive symptoms. The findings of this study were that amongst this sample, those who had higher levels of depressive

symptoms also had longer DFU healing time. Therefore, the first hypothesis, was supported. Major levels of depressive symptoms were found to be associated with DFU healing times 3.5 times longer than people with a DFU and no depressive symptoms.

The second aim, to determine if there is a relationship between different levels of depressive symptoms and different levels of T2D in a population with a DFU was explored. To investigate this aim, it was hypothesised that people with high levels of depressive symptoms will have higher levels of T2D. This study found that there was a relationship between different levels of depressive symptoms and T2D, and thus the second hypothesis was supported. In further exploring this relationship, it was hypothesised that there would be a mediating effect of T2D on the relationship between depressive symptoms and DFU healing time. Different T2D levels were found to have no relationship with the healing time of a DFU themselves, while T2D was found to influence the relationship between depression and healing time moderately and to a level of 21%. This result supports this hypothesis, that there is a mediating influence of T2D on the relationship between depressive symptoms and DFU healing time, however it was found to be low.

The third aim was to determine if there is a relationship between depressive symptoms and the QoL amongst a population with a DFU. To investigate this aim, it was hypothesised that among a population with a DFU, higher levels of depressive symptoms would correlate with lower levels of QoL. The results of this study established that there was a variance across the different levels of depressive symptoms, with all levels of depression having a relationship with both healing time and individuals QoL. This hypothesis was supported, as significant correlations were found between depressive symptoms and individuals QoL. The results of this study did establish that the QoL amongst a sample with a DFU was considerably lower when compared to Australian population norms. Both depression and T2D negatively impacted across all domains of QoL, with depressive symptoms having a stronger relationship and influence on individuals QoL when compared to T2D.

The clinical significance of these findings is particularly relevant. When considering how depressive symptoms may influence both healing time and individuals QoL amongst people with a DFU, no matter what level of T2D is present. It was found that more than half had some level of depressive symptoms, and the higher the T2D, the higher the level of depression. Clinically, the current best practice guidelines do not specifically consider the impact depression has on the ability to heal a DFU. The importance of this finding is particularly relevant considering that when treating a DFU, the current best practice approach has been to focus on managing and improving the T2D levels and use a medical or biological treatment approach of the foot ulcer; rather than considering a more holistic treatment approach which includes consideration of mental health influences. The current research suggests that by adopting a treatment plan that includes addressing depressive symptoms that may be present, it may be possible to influence DFU healing time. This is important when considering the major cost and length of treatment time DFUs have on the health system, not only in Australia but worldwide.

An interesting finding was that there was no relationship between the level of T2D and healing time. This could be due to the many influencing factors previously mentioned on achieving successful DFU healing. Type 2 diabetes alone, irrespective of diabetes level, did not specifically relate to the observed healing time in this sample. However, this result is not to discount the importance in managing T2D by attempting to better control levels of blood glucose when treating a DFU. A possible conclusion however to be drawn from this study is that, different levels of T2D did not appear to influence the rate of DFU healing. Therefore more emphasis is required to manage the other compounding influences, in order to improve overall healing time of DFUs.

Managing T2D alone has an impact on an individual's life, yet when the debilitating effect of a DFU is added, this study shows how an individual's mental health may be

negatively impacted. Consideration of how an improvement in any one of QoL, T2D level or depressive symptoms may have on each other, and how improvements on any single one may have a dramatic and beneficial influence amongst this population. The integration of mental health specialists to specifically treat depressive symptoms within the patient population of all HRFS or any diabetic service, particularly where the treatment of ulcers occurs would be beneficial. Further an increased attention and focus on patient's QoL may influence DFU healing times. The current attention to specifically treating T2D as a key influencer on healing rates amongst this population should continue, and this study reinforces the best practice of a multidisciplinary approach to managing DFUs; however, more emphasis should be provided to treating the depressive symptoms that are highly prevalent amongst this population, as well as an emphasis on how support to patients to improve facets of their QoL. By increasing the focus on these two areas; depression and QoL instead of just the medical model of direct ulcer treatment and managing the T2D, it may be possible to further influence the healing rate of a DFU, and thus influence the overall cost to the health system. There is no doubt on the impact a DFU has on an individual, the QoL comparisons with established norms highlight this; what is clear from this study, is that there are broader influences on DFU healing rates than just T2D. Depression levels, and the individuals QoL have a direct relationship with the time it takes to heal a DFU. The overall aim of managing and treating a DFU is to achieve long term healing in the shortest time. It is evident that the best DFU treatment outcomes cannot be achieved with a treatment model focusing on T2D management without consideration of the relationship depressive symptoms and QoL both have.

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Northern Health

27th March 2013

Mr Andrew Steel
Orthotics Department
Northern Health

Dear Andrew,

RE: LR 10/13 Relationship between depression on quality of life and foot ulcer healing rates in type 2 diabetic (T2DM) patients with a neuropathic foot ulcer.

The above project has been reviewed by the NH Research Ethics committee and is approved to commence on 01 July 2013

The approved version of the patient information sheet is dated 27.06.2013.

This project has been approved until June 2015. Please note that the NH HREC and Research Governance Office require an annual progress report to be submitted in July each year.

Yours sincerely,


Anastasia Hutchinson

Chair of the Low Risk Ethics Committee
NORTHERN HEALTH

